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NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	Jun 03	New e-mail delivery for search results now available
NEWS 4	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11	Oct 24	BEILSTEIN adds new search fields
NEWS 12	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13	Nov 18	DKILIT has been renamed APOLLIT
NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
NEWS 16	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17	Dec 17	TOXCENTER enhanced with additional content
NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
NEWS 21	Feb 24	METADEX enhancements
NEWS 22	Feb 24	PCTGEN now available on STN
NEWS 23	Feb 24	TEMA now available on STN
NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 20	EVENTLINE will be removed from STN
NEWS 28	Mar 24	PATDPAFULL now available on STN
NEWS 29	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 30	Apr 11	Display formats in DGENE enhanced
NEWS 31	Apr 14	MEDLINE Reload
NEWS 32	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 33	Jun 13	Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35	Apr 28	RDISCLOSURE now available on STN
NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
NEWS 37	May 15	MEDLINE file segment of TOXCENTER reloaded
NEWS 38	May 15	Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39	May 16	CHEMREACT will be removed from STN
NEWS 40	May 19	Simultaneous left and right truncation added to WSCA
NEWS 41	May 19	RAPRA enhanced with new search field, simultaneous left and right truncation
NEWS 42	Jun 06	Simultaneous left and right truncation added to CBNB

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 NEWS 43  Jun 06  PASCAL enhanced with additional data
 NEWS 44  Jun 20  2003 edition of the FSTA Thesaurus is now available

 NEWS EXPRESS  April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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=> file medline, uspatful, dgene, embase, scisearch, wpids, biosis, fsta, jicst,
hcaplus, japio
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FILE 'USPATFULL' ENTERED AT 16:19:34 ON 23 JUN 2003
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FILE 'JAPIO' ENTERED AT 16:19:34 ON 23 JUN 2003
COPYRIGHT (C) 2003 Japanese Patent Office (JPO)- JAPIO
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=> s lactacystin
L1         3668 LACTACYSTIN

=> s dipeptide boronic acid or DPBA
L2          243 DIPEPTIDE BORONIC ACID OR DPBA

=> s proteasome inhibitor
L3         4499 PROTEASOME INHIBITOR

=> s l3 and activated blood cells
L4            2 L3 AND ACTIVATED BLOOD CELLS

=> d l4 ti abs ibib tot

L4   ANSWER 1 OF 2  USPATFULL
TI     Use of proteasome inhibitors for treating cancer, inflammation,
       autoimmune disease, graft rejection and septic shock
AB     The present invention relates to compositions comprising proteasome
       inhibitors, such as lactacystin, DPBA and their analogs. These
       compositions are used for the following purposes: (1) to disrupt
       mitochondrial function (useful aganst cancer, inflammation, adverse
       immune reaction and hyperthyroidism), (2) to disrupt nitric oxide
       synthesis (useful against inflammation and septic shock), and (3) to
       reverse ongoing adverse immune reactions, such as autoimmune diseases
       and graft rejection. In the later case, the compositions can be
       administered once the patients' T cells are mostly activated. Proteasome
       inhibitors can also be combined to immuno-suppressinve drugs like
       rapamycin, cyclosporin A and FK506. Finally, a method for screening a
       compound having a proteasome inhibition activity is also disclosed and
       claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER:        2002:92633  USPATFULL
TITLE:                   Use of proteasome inhibitors for treating cancer,
                         inflammation, autoimmune disease, graft rejection and
                         septic shock
INVENTOR(S):             Wu, Jiangping, Brossard, CANADA
                         Wang, Xin, Montreal, CANADA

                              NUMBER        KIND    DATE
                         ---------------- ------ --------
PATENT INFORMATION:      US 2002049157      A1   20020425
APPLICATION INFO.:       US 2001-904251     A1   20010712  (9)
RELATED APPLN. INFO.:    Continuation-in-part of Ser. No. US 1999-341009, filed
                         on 25 Aug 1999, PENDING A 371 of International Ser. No.
                         WO 1998-CA1010, filed on 29 Oct 1998, UNKNOWN

                                NUMBER         DATE
                         ------------------ --------
PRIORITY INFORMATION:    US 2000-218145P    20000714 (60)
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN,
                         55402-0903
NUMBER OF CLAIMS:        12
EXEMPLARY CLAIM:         1
NUMBER OF DRAWINGS:      34 Drawing Page(s)
LINE COUNT:              2010
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4   ANSWER 2 OF 2  WPIDS (C) 2003 THOMSON DERWENT
TI   Use of a proteasome inhibitor for reversing
     proliferation or activity of activated blood
```

cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.

AN 2002-507279 [54] WPIDS

CR 1999-313169 [26]

AB US2002049157 A UPAB: 20020823

NOVELTY - A novel method for reversing an ongoing proliferation or activity, or both, of **activated blood cells**, comprises administering a **proteasome inhibitor** to an individual.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antibacterial; Cytostatic.

MECHANISM OF ACTION - **Proteasome inhibitor**; inhibitors of CDK2 and Cyclin E.

The role of proteasome in T cell activation and proliferation was first examined in PBMC, using the proteasome-specific inhibitor LAC. The peripheral blood mononuclear cells (PBMC) were activated with various stimulants. LAC was added to the cells in the beginning of the culture (0 hours) along with the stimulants. 3H-thymidine uptake between 48 and 64 hours of 64 hour cultures was used as a parameter for cell proliferation. LAC strongly and dose-dependently inhibited the T cell proliferation induced by a T cell mitogen PHA by crosslinking TCR with anti-CD3 E, or by Ca++ ionophore plus cross-linking of the T cell co-stimulating molecule CD28. The T-cell-independent B cell proliferation induced with SAC plus IL-2 in tonsillar B cells was also potently inhibited by LAC. In all systems used, LAC at 5 micro M could exert near-to-maximal inhibition. The results suggest that LACs effect is not lymphocyte type (T or B cells)-specific nor stimulant-specific. It likely affects certain down-stream events governing a more general process in lymphocyte activation and proliferation.

USE - The methods can be used for treating an adverse immune response such as an autoimmune disease or a graft rejection, or inflammation or septic shock (claimed). The methods can be used for reversing an ongoing proliferation or activity which may result in **activated blood cells** apoptosis, or inhibition of energy and oxygen supply to the **activated blood cells**, or where the inhibition of energy and oxygen supply is caused by disrupting mitochondrial function in **activated blood cells** or disruption of nitric acid synthesis (claimed). The methods can also be used for treating e.g. cancers, hyperthyroidisn and graft rejection.

The use of DPBA in organ transplantation-islet graft in streptozocin-induced diabetes in mice was studied. Islets from Balb/c mice in diabetic C57BL/6 recipients were used. The islets from syngeneic mice (isograft control) restored normal glycemia in diabetic mice, and the effect lasted more than 60 days as expected. The allogenic islets were rejected in about 10 days in untreated mice, and the mice became diabetic after an initial dip of their blood sugar level (allograft control). When the allogenic islets were transplanted to diabetic recipients along with DPBA treatment, the graft functioned normally beyond 60 days, indicating that the graft rejection was inhibited. This result showed that proteasome inhibitors as exemplified by DPBA can be used in human islet transplantation to prevent graft rejection. It was shown that a **proteasome inhibitor** such as DPBA inhibits the glucose elevation consequent to islet rejection.

ADVANTAGE - The proteasome inhibitors such as LAC and DPBA have shown an unique capacity to reverse an ongoing activity of blood cells. This reversal makes the possibility of treatment which selectively targets **activated blood cells**. The protease inhibitor are responsible for preventing allograft rejection for the first time successfully. Also an effective screening method for searching for other proteasome inhibitors has been found.

Dwg.0/31

ACCESSION NUMBER: 2002-507279 [54] WPIDS

CROSS REFERENCE: 1999-313169 [26]

DOC. NO. CPI: C2002-144189
TITLE: Use of a **proteasome inhibitor** for reversing proliferation or activity of **activated blood cells** for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
DERWENT CLASS: B04 B05
INVENTOR(S): WANG, X; WU, J
PATENT ASSIGNEE(S): (WANG-I) WANG X; (WUJJ-I) WU J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002049157	A1	20020425	(200254)*		54

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2002049157	A1	CIP of	WO 1998-CA1010	19981029
		CIP of	US 1999-341009	19990825
		Provisional	US 2000-218145P	20000714
			US 2001-904251	20010712

PRIORITY APPLN. INFO: US 2000-218145P 20000714; WO 1998-CA1010 19981029; US 1999-341009 19990825; US 2001-904251 20010712

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FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, SCISEARCH, WPIDS, BIOSIS, FSTA, JICST-EPLUS, HCAPLUS, JAPIO' ENTERED AT 16:19:34 ON 23 JUN 2003
L1 3668 S LACTACYSTIN
L2 243 S DIPEPTIDE BORONIC ACID OR DPBA
L3 4499 S PROTEASOME INHIBITOR
L4 2 S L3 AND ACTIVATED BLOOD CELLS

=> s l1 and proliferation
L5 281 L1 AND PROLIFERATION

=> d l2 and proliferation
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=> s l2 and proliferation
L6 22 L2 AND PROLIFERATION

=> s l5 and l6
L7 3 L5 AND L6

=> d l7 ti abs ibib tot

L7 ANSWER 1 OF 3 USPATFULL
TI Use of proteasome inhibitors for treating cancer, inflammation,

autoimmune disease, graft rejection and septic shock

AB The present invention relates to compositions comprising proteasome inhibitors, such as **lactacystin**, **DPBA** and their analogs. These compositions are used for the following purposes: (1) to disrupt mitochondrial function (useful aganst cancer, inflammation, adverse immune reaction and hyperthyroidism), (2) to disrupt nitric oxide synthesis (useful against inflammation and septic shock), and (3) to reverse ongoing adverse immune reactions, such as autoimmune diseases and graft rejection. In the later case, the compositions can be administered once the patients' T cells are mostly activated. Proteasome inhibitors can also be combined to immuno-suppressinve drugs like rapamycin, cyclosporin A and FK506. Finally, a method for screening a compound having a proteasome inhibition activity is also disclosed and claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2002:92633 USPATFULL
TITLE:	Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock
INVENTOR(S):	Wu, Jiangping, Brossard, CANADA Wang, Xin, Montreal, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002049157	A1	20020425
APPLICATION INFO.:	US 2001-904251	A1	20010712 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-341009, filed on 25 Aug 1999, PENDING A 371 of International Ser. No. WO 1998-CA1010, filed on 29 Oct 1998, UNKNOWN

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NUMBER OF CLAIMS:	12
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	34 Drawing Page(s)
LINE COUNT:	2010

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 2 OF 3 SCISEARCH COPYRIGHT 2003 THOMSON ISI

TI A proteasome inhibitor effectively prevents mouse heart allograft rejection

AB Background. We have previously demonstrated in vitro that proteasome inhibitors could suppress **proliferation** and induce apoptosis of activated T cells. This finding suggests that such inhibitors could be used as a novel category of immunosuppressants in blocking allograft rejection.

Methods. The proteasome inhibitor **dipeptide boronic . acid** (**DPBA**) was tested in vitro for its inhibitory effect on mouse T-cell **proliferation** and lymphokine secretion. **DPBA** was also used in vivo to treat mouse heterotopic heart allograft rejection. Possible side effects of this compound were examined according to blood chemistry of mice treated with **DPBA**.

Results, **DPBA** suppressed the T-cell **proliferation** and potently inhibited interleukin (IL)-2, IL-6, IL-10, IL-13, and IFN-gamma produced by anti-CD3-activated T cells. Given i.p. starting I day after transplantation at 0.66 mg/kg per day for 16 days, or at I mg(kg per day for 4 days followed by 0.5 mg/kg per day for 12 days, **DPBA** could prolong heart allograft survival to 35.5 days (mean survival time,

MST) and to 36.2 days, respectively. The control group had MST of 7.3 days. When administrated 72 hr post operation at I mg/kg per day for 4 days, **DPBA** could prolong the graft survival to 19.8 days. During the course of these effective dosages, **DPBA** had no apparent toxicity in the liver, kidney, pancreas, or heart, according to analysis of blood chemistry.

Conclusions. The proteasome inhibitor could repress allograft rejection in mice without apparent side-effects at the effective dosages. This finding has opened a new dimension in development of novel immunosuppressants for organ transplantation.

ACCESSION NUMBER: 2001:657648 SCISEARCH
THE GENUINE ARTICLE: 461AK
TITLE: A proteasome inhibitor effectively prevents mouse heart allograft rejection
AUTHOR: Luo H Y; Wu Y L; Qi S J; Wan X C; Chen H F; Wu J P (Reprint)
CORPORATE SOURCE: CHUM, Notre Dame Hosp, Res Ctr, Lab Transplantat Immunol, 1560 Sherbrooke St, Pavilion De Seve, Rm Y-5612, Montreal, PQ H2L 4M1, Canada (Reprint); CHUM, Notre Dame Hosp, Res Ctr, Lab Transplantat Immunol, Montreal, PQ H2L 4M1, Canada; Univ Montreal, Notre Dame Hosp, CHUM, Nephrol Serv, Montreal, PQ H3C 3J7, Canada; McGill Univ, Dept Surg, Montreal, PQ, Canada; Zhejiang Univ, Affiliated Hosp 2, Sch Med, Dept Surg, Zhenjiang, Peoples R China
COUNTRY OF AUTHOR: Canada; Peoples R China
SOURCE: TRANSPLANTATION, (27 JUL 2001) Vol. 72, No. 2, pp. 196-202

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.
ISSN: 0041-1337.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 24
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L7 ANSWER 3 OF 3 WPIDS (C) 2003 THOMSON DERWENT
TI Use of a proteasome inhibitor for reversing **proliferation** or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
AN 2002-507279 [54] WPIDS
CR 1999-313169 [26]
AB US2002049157 A UPAB: 20020823
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ADVANTAGE - The proteasome inhibitors such as LAC and **DPBA** have shown an unique capacity to reverse an ongoing activity of blood cells. This reversal makes the possibility of treatment which selectively targets activated blood cells. The protease inhibitor are responsible for preventing allograft rejection for the first time successfully. Also an effective screening method for searching for other proteasome inhibitors has been found.

Dwg.0/31

ACCESSION NUMBER: 2002-507279 [54] WPIDS
CROSS REFERENCE: 1999-313169 [26]
DOC. NO. CPI: C2002-144189
TITLE: Use of a proteasome inhibitor for reversing **proliferation** or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
DERWENT CLASS: B04 B05
INVENTOR(S): WANG, X; WU, J
PATENT ASSIGNEE(S): (WANG-I) WANG X; (WUJJ-I) WU J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002049157	A1	20020425	(200254)*		54

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2002049157	A1	CIP of	WO 1998-CA1010	19981029
		CIP of	US 1999-341009	19990825
		Provisional	US 2000-218145P	20000714
			US 2001-904251	20010712

PRIORITY APPLN. INFO: US 2000-218145P 20000714; WO 1998-CA1010 19981029; US 1999-341009 19990825; US 2001-904251 20010712

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     FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, SCISEARCH, WPIDS, BIOSIS, FSTA,
     JICST-EPLUS, HCAPLUS, JAPIO' ENTERED AT 16:19:34 ON 23 JUN 2003
L1          3668 S LACTACYSTIN
L2           243 S DIPEPTIDE BORONIC ACID OR DPBA
L3          4499 S PROTEASOME INHIBITOR
L4             2 S L3 AND ACTIVATED BLOOD CELLS
L5           281 S L1 AND PROLIFERATION
L6            22 S L2 AND PROLIFERATION
L7             3 S L5 AND L6

=> s l6 and inhibition
L8            14 L6 AND INHIBITION

=> s l5 and inhibition
L9           176 L5 AND INHIBITION

=> d l8 ti abs ibib tot

L8   ANSWER 1 OF 14      MEDLINE
TI   Mechanisms of Proteasome Inhibitor PS-341-induced G(2)-M-Phase Arrest and
     Apoptosis in Human Non-Small Cell Lung Cancer Cell Lines.
AB   PURPOSE: PS-341 is a novel dipeptide boronic
     acid proteasome inhibitor with in vitro and in vivo antitumor
     activity that induces mechanisms of apoptosis by unknown mechanisms.
     Experimental Design: Human non-small cell lung cancer cell lines were used
     to investigate effects PS-341 on cell proliferation, cell cycle
     progression, and the induction of apoptosis. RESULTS: PS-341 was
     38-360-fold more cytotoxic against H460 cells when compared with the
     proteasome inhibitors MG-132 and PSI. Differential PS-341 cytotoxic
     effects were found with respect to P53 function: H322 cells (p53 mutant)
     were 6-fold less sensitive as compared with H460 cells (p53 wild type);
     and H358 cells (p53 null) were 1.6-fold more sensitive as compared with
     H460 cells (p53 wild type). A concentration- and time-dependent cell
     cycle blockade at G(2)-M phase was seen for H460 cells without any direct
     effects on microtubule polymerization or depolymerization. PS-341
     exposure in H460 cells led to stabilization of p53, induction of
     p21(cip/waf-1) and MDM2 expression, an increase in cyclin B and cyclin A,
     and the activation of cyclin B and cyclin A kinases. MDM2 induction was
     found only in H460 cells, whereas in H322 and H358 cells, G(2)-M-phase
     arrest, p21(cip/waf-1) induction, and an increase in cyclin B1 were found.
     The commitment of G(2)-M-phase cells to apoptosis was verified by the
     activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase in
     drug-free medium. CONCLUSIONS: Our data suggest that the PS-341-induced
     G(2)-M-phase arrest may be associated with the inhibition of
     degradation of cell cycle regulators and that the up-regulation of
     p21(cip/waf-1) expression may be via p53-dependent and/or -independent
     pathways. The resulting disturbance of cell cycle progression leads
     either to growth inhibition or to the initiation of apoptotic
     pathways.
ACCESSION NUMBER:    2003118034      IN-PROCESS
DOCUMENT NUMBER:     22518387   PubMed ID: 12631620
TITLE:               Mechanisms of Proteasome Inhibitor PS-341-induced
                     G(2)-M-Phase Arrest and Apoptosis in Human Non-Small Cell
                     Lung Cancer Cell Lines.
AUTHOR:              Ling Yi-He; Liebes Leonard; Jiang Jian-Dong; Holland James
                     F; Elliott Peter J; Adams Julian; Muggia Franco M;
                     Perez-Soler Roman
CORPORATE SOURCE:    Department of Oncology, Albert Einstein College of
                     Medicine, Bronx, New York 10461 [Y-H. L., R. P-S.].
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SOURCE: CLINICAL CANCER RESEARCH, (2003 Mar) 9 (3) 1145-54.
Journal code: 9502500. ISSN: 1078-0432.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030313
Last Updated on STN: 20030313

L8 ANSWER 2 OF 14 MEDLINE
TI 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer.
AB The 26S proteasome degrades proteins that regulate transcription factor activation, cell cycle progression, and apoptosis. In cancer, this may allow for uncontrolled cell division, promoting tumor growth, and spread. We examined whether selective **inhibition** of the 26S proteasome with PS-341, a **dipeptide boronic acid** analogue, would block **proliferation** and induce apoptosis in human pancreatic cancer. Proteasome **inhibition** significantly blocked mitogen (FCS) induced **proliferation** of BxPC3 human pancreatic cancer cells in vitro, while arresting cell cycle progression and inducing apoptosis by 24 h. Accumulation of p21(Cip1-Waf-1), a cyclin dependent kinase (CDK) inhibitor normally degraded by the 26S proteasome, occurred by 3 h and correlated with cell cycle arrest. When BxPC3 pancreatic cancer xenografts were established in athymic nu/nu mice, weekly administration of 1 mg/kg PS-341 significantly inhibited tumor growth. Both cellular apoptosis and p21(Cip1-Waf-1) protein levels were increased in PS-341 treated xenografts. **Inhibition** of tumor xenograft growth was greatest (89%) when PS-341 was combined with the tumoricidal agent CPT-11. Combined CPT-11/PS-341 therapy, but not single agent therapy, yielded highly apoptotic tumors, significantly inhibited tumor cell **proliferation**, and blocked NF-kappaB activation indicating this systemic therapy was effective at the cancer cell level. 26S proteasome **inhibition** may represent a new therapeutic approach against this highly resistant and lethal malignancy.

ACCESSION NUMBER: 2001331410 MEDLINE
DOCUMENT NUMBER: 21293160 PubMed ID: 11400168
TITLE: 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer.
AUTHOR: Shah S A; Potter M W; McDade T P; Ricciardi R; Perugini R A; Elliott P J; Adams J; Callery M P
CORPORATE SOURCE: Department of Surgery, University of Massachusetts Medical School, Worcester, Massachusetts, USA.
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (2001 Apr 2-27) 82 (1) 110-22.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010924
Last Updated on STN: 20030313
Entered Medline: 20010920

L8 ANSWER 3 OF 14 USPATFULL
TI Method of preventing T cell-mediated responses by the use of the major histocompatibility complex class II analog protein (map protein) from Staphylococcus aureus
AB A method of immunomodulating the T cell response in Staphylococcal bacteria is provided wherein an effective amount of the Map protein from Staphylococcus aureus is administered to a host to prevent or suppress the T cell response. The present method may be utilized with either the

Map protein or an effective subdomain or fragment thereof such as the Map 10 or Map 19 protein. The present invention is advantageous in that suppression or prevention of the T cell response in a host can prevent or ameliorate a wide variety of the pathogenic conditions such as T cell lymphoproliferative disease and toxic shock syndrome wherein the overstimulation of T cells needs to be suppressed or modulated.

ACCESSION NUMBER: 2003:158951 USPATFULL
TITLE: Method of preventing T cell-mediated responses by the use of the major histocompatibility complex class II analog protein (map protein) from Staphylococcus aureus
INVENTOR(S): Brown, Eric, Houston, TX, UNITED STATES
Lee, Lawrence, Houston, TX, UNITED STATES
Hook, Magnus, Houston, TX, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2003108564	A1	20030612	
APPLICATION INFO.:	US 2002-41775	A1	20020110	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-260523P	20010110 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: LARSON & TAYLOR, PLC, 1199 NORTH FAIRFAX STREET, SUITE 900, ALEXANDRIA, VA, 22314
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1439

L8 ANSWER 4 OF 14 USPATFULL
TI Diagnosing and treating cancer cells using Sal2
AB The invention features the use of Sal2 nucleic acids and proteins in methods for treating patients having proliferative disorders, such as cancers, involving mutations in a Sal2 nucleic acid sequence and in the protein that it encodes. In addition, these treatment methods may also be used for patients having a mutation in a nucleic acid sequence encoding a protein that interacts with Sal2 or that functions in a signaling pathway involving Sal2. Furthermore, Sal2 may be used as an anti-viral agent that interferes with the ability of a DNA tumor virus to replicate and disseminate in a cell.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:280594 USPATFULL
TITLE: Diagnosing and treating cancer cells using Sal2
INVENTOR(S): Benjamin, Thomas L., Cambridge, MA, UNITED STATES
Li, Dawei, Boston, MA, UNITED STATES
Mok, Samuel C., Brookline, MA, UNITED STATES
Cramer, Daniel W., Chestnut Hill, MA, UNITED STATES
Ma, Yupo, Sharon, MA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002156039	A1	20021024	
APPLICATION INFO.:	US 2001-988117	A1	20011116	(9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-812633, filed on 19 Mar 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-216723P	20000707 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110
NUMBER OF CLAIMS: 10
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 11 Drawing Page(s)
LINE COUNT: 2667
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 5 OF 14 USPATFULL
TI Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock
AB The present invention relates to compositions comprising proteasome inhibitors, such as lactacystin, **DPBA** and their analogs. These compositions are used for the following purposes: (1) to disrupt mitochondrial function (useful aganst cancer, inflammation, adverse immune reaction and hyperthyroidism), (2) to disrupt nitric oxide synthesis (useful against inflammation and septic shock), and (3) to reverse ongoing adverse immune reactions, such as autoimmune diseases and graft rejection. In the later case, the compositions can be administered once the patients' T cells are mostly activated. Proteasome inhibitors can also be combined to immuno-suppressinve drugs like rapamycin, cyclosporin A and FK506. Finally, a method for screening a compound having a proteasome **inhibition** activity is also disclosed and claimed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2002:92633 USPATFULL
TITLE: Use of proteasome inhibitors for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock
INVENTOR(S): Wu, Jiangping, Brossard, CANADA
Wang, Xin, Montreal, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002049157	A1	20020425
APPLICATION INFO.:	US 2001-904251	A1	20010712 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-341009, filed on 25 Aug 1999, PENDING A 371 of International Ser. No. WO 1998-CA1010, filed on 29 Oct 1998, UNKNOWN

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-218145P	20000714 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCHANT & GOULD PC, P.O. BOX 2903, MINNEAPOLIS, MN, 55402-0903
NUMBER OF CLAIMS: 12
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 34 Drawing Page(s)
LINE COUNT: 2010
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8 ANSWER 6 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Mechanisms of proteasome inhibitor PS-341-induced G(2)-M-phase arrest and apoptosis in human non-small cell lung cancer cell lines.
AB Purpose: PS-341 is a novel **dipeptide boronic acid** proteasome inhibitor with in vitro and in vivo antitumor activity that induces mechanisms of apoptosis by unknown mechanisms. Experimental Design: Human non-small cell lung cancer cell lines were used to investigate effects PS-341 on cell **proliferation**, cell cycle progression, and the induction of apoptosis. Results: PS-341 was

38-360-fold more cytotoxic against H460 cells when compared with the proteasome inhibitors MG-132 and PSI. Differential PS-341 cytotoxic effects were found with respect to P53 function: H322 cells (p53 mutant) were 6-fold less sensitive as compared with H460 cells (p53 wild type); and H358 cells (p53 null) were 1.6-fold more sensitive as compared with H460 cells (p53 wild type). A concentration- and time-dependent cell cycle blockade at G(2)-M phase was seen for H460 cells without any direct effects on microtubule polymerization or depolymerization. PS-341 exposure in H460 cells led to stabilization of p53, induction of p21(cip/waf-1) and MDM2 expression, an increase in cyclin B and cyclin A, and the activation of cyclin B and cyclin A kinases. MDM2 induction was found only in H460 cells, whereas in H322 and H358 cells, G(2)-M-phase arrest, p21(cip/waf-1) induction, and an increase in cyclin B1 were found. The commitment of G(2)-M-phase cells to apoptosis was verified by the activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase in drug-free medium. Conclusions: Our data suggest that the PS-341-induced G(2)-M-phase arrest may be associated with the **inhibition** of degradation of cell cycle regulators and that the up-regulation of p21(cip/waf-1) expression may be via p53-dependent and/or -independent pathways. The resulting disturbance of cell cycle progression leads either to growth **inhibition** or to the initiation of apoptotic pathways.

ACCESSION NUMBER: 2003116839 EMBASE
TITLE: Mechanisms of proteasome inhibitor PS-341-induced G(2)-M-phase arrest and apoptosis in human non-small cell lung cancer cell lines.
AUTHOR: Ling Y.-H.; Liebes L.; Jiang J.-D.; Holland J.F.; Elliott P.J.; Adams J.; Muggia F.M.; Perez-Soler R.
CORPORATE SOURCE: R. Perez-Soler, Department of Oncology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461, United States. rperezso@montefiore.org
SOURCE: Clinical Cancer Research, (1 Mar 2003) 9/3 (1145-1154). Refs: 36
ISSN: 1078-0432 CODEN: CCREF4
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 7 OF 14 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer.
AB The 26S proteasome degrades proteins that regulate transcription factor activation, cell cycle progression, and apoptosis. In cancer, this may allow for uncontrolled cell division, promoting tumor growth, and spread. We examined whether selective **inhibition** of the 26S proteasome with PS-341, a **dipeptide boronic acid** analogue, would block **proliferation** and induce apoptosis in human pancreatic cancer. Proteasome **inhibition** significantly blocked mitogen (FCS) induced **proliferation** of BxPC3 human pancreatic cancer cells in vitro, while arresting cell cycle progression and inducing apoptosis by 24 h. Accumulation of p21(Cip1-Waf-1), a cyclin dependent kinase (CDK) inhibitor normally degraded by the 26S proteasome, occurred by 3 h and correlated with cell cycle arrest. When BxPC3 pancreatic cancer xenografts were established in athymic nu/nu mice, weekly administration of 1 mg/kg PS-341 significantly inhibited tumor growth. Both cellular apoptosis and p21(Cip1-Waf-1) protein levels were increased in PS-341 treated xenografts. **Inhibition** of tumor xenograft growth was greatest (89%) when PS-341 was combined with the tumoricidal agent CPT-11. Combined CPT-11/PS-341 therapy, but not single agent therapy, yielded highly apoptotic tumors, significantly inhibited tumor cell **proliferation**, and blocked NF-.kappa.B activation

indicating this systemic therapy was effective at the cancer cell level. 26S proteasome **inhibition** may represent a new therapeutic approach against this highly resistant and lethal malignancy. .COPYRGT. 2001 Wiley-Liss, Inc.

ACCESSION NUMBER: 2001198191 EMBASE
TITLE: 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer.
AUTHOR: Shah S.A.; Potter M.W.; McDade T.P.; Ricciardi R.; Perugini R.A.; Elliott P.J.; Adams J.; Callery M.P.
CORPORATE SOURCE: M.P. Callery, Univ. of Massachusetts Med. School, 55 Lake Avenue North, Worcester, MA 01655, United States. callerym@ummhc.org
SOURCE: Journal of Cellular Biochemistry, (2001) 82/1 (110-122). Refs: 44
ISSN: 0730-2312 CODEN: JCEBD5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 8 OF 14 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI Mechanisms of proteasome inhibitor PS-341-induced G(2)-M-phase arrest and apoptosis in human non-small cell lung cancer cell lines
AB Purpose: PS-341 is a novel **dipeptide boronic acid** proteasome-inhibitor with in vitro and in vivo antitumor activity that induces mechanisms of apoptosis by unknown mechanisms.

Experimental Design: Human non-small cell lung cancer cell lines were used to investigate effects PS-341 on cell **proliferation**, cell cycle progression, and the induction of apoptosis.

Results: PS-341 was 38-360-fold more cytotoxic against H460 cells when compared with the proteasome inhibitors MG-132 and PSI. Differential PS-341 cytotoxic effects were found with respect to P53 function: H322 cells (p53 mutant) were 6-fold less sensitive as compared with H460 cells (p53 wild type); and H358 cells (p53 null) were 1.6-fold more sensitive as compared with H460 cells (p53 wild type). A concentration- and time-dependent cell cycle blockade at G.-M phase was seen for H460 cells without any direct effects on microtubule polymerization or depolymerization. PS-341 exposure in H460 cells led to stabilization of p53, induction of p21(cip/waf-1) and MDM2 expression, an increase in cyclin B and cyclin A, and the activation of cyclin B and cyclin A kinases. MDM2 induction was found only in H460 cells, whereas in H322 and H358 cells, G(2)-M-phase arrest, p21(cip/waf-1) induction, and an increase in cyclin B1 were found. The commitment of G2-M-phase cells to apoptosis was verified by the activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase in drug-free medium.

Conclusions: Our data suggest that the PS-341-induced G(2)-M-phase arrest may be associated with the **inhibition** of degradation of cell cycle regulators and that the up-regulation of p21(cip/waf-1) expression may be via p53-dependent and/or -independent pathways. The resulting disturbance of cell cycle progression leads either to growth **inhibition** or to the initiation of apoptotic pathways.

ACCESSION NUMBER: 2003:231647 SCISEARCH
THE GENUINE ARTICLE: 653JA
TITLE: Mechanisms of proteasome inhibitor PS-341-induced G(2)-M-phase arrest and apoptosis in human non-small cell lung cancer cell lines
AUTHOR: Ling Y H; Liebes L; Jiang J D; Holland J F; Elliott P J; Adams J; Muggia F M; Perez-Soler R (Reprint)
CORPORATE SOURCE: Albert Einstein Coll Med, Dept Oncol, 1300 Morris Pk Ave, Bronx, NY 10461 USA (Reprint); Albert Einstein Coll Med,

Dept Oncol, Bronx, NY 10461 USA; NYU, Sch Med, Kaplan Comprehens Canc Ctr, New York, NY 10016 USA; Mt Sinai Sch Med, Dept Med, New York, NY 10029 USA; Millennium Pharmaceut Inc, Cambridge, MA 02139 USA
COUNTRY OF AUTHOR: USA
SOURCE: CLINICAL CANCER RESEARCH, (MAR 2003) Vol. 9, No. 3, pp. 1145-1154.
Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806, BIRMINGHAM, AL 35202 USA.
ISSN: 1078-0432.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L8 ANSWER 9 OF 14 SCISEARCH COPYRIGHT 2003 THOMSON ISI
TI 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer
AB The 26S proteasome degrades proteins that regulate transcription factor activation, cell cycle progression, and apoptosis. In cancer, this may allow for uncontrolled cell division, promoting turner growth, and spread. We examined whether selective **inhibition** of the 26S proteasome with PS-341, a **dipeptide boronic acid** analogue, would block **proliferation** and induce apoptosis in human pancreatic cancer. Proteasome **inhibition** significantly blocked mitogen (FCS) induced **proliferation** of BxPC3 human pancreatic cancer cells in vitro, while arresting cell cycle progression and inducing apoptosis by 24 h. Accumulation of p21(Cip1-Waf-1), a cyclin dependent kinase (CDK) inhibitor normally degraded by the 26S proteasome, occurred by 3 h and correlated with cell cycle arrest. When BxPC3 pancreatic cancer xenografts were established in athymic nu/nu mice, weekly administration of 1 mg/kg PS-341 significantly inhibited rumor growth. Both cellular apoptosis and p21(Cip1-Waf-1) protein levels were increased in PS-341 treated xenografts. **Inhibition** of tumor xenograft growth was greatest (89%) when PS-341 was combined with the tumoricidal agent CPT-11. Combined CPT-11/PS-341 therapy, but not single agent therapy, yielded highly apoptotic tumors, significantly inhibited turner cell **proliferation**, and blocked NF-kappaB activation indicating this systemic therapy was effective at the cancer cell level. 26S proteasome **inhibition** may represent a new therapeutic approach against this highly resistant and lethal malignancy.
ACCESSION NUMBER: 2001:467077 SCISEARCH
THE GENUINE ARTICLE: 438JG
TITLE: 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer
AUTHOR: Shah S A; Potter M W; McDade T P; Ricciardi R; Perugini R A; Elliott P J; Adams J; Callery M P (Reprint)
CORPORATE SOURCE: Univ Massachusetts, Sch Med, Dept Surg, 55 Lake Ave N, Worcester, MA 01655 USA (Reprint); Univ Massachusetts, Sch Med, Dept Surg, Worcester, MA 01655 USA; Univ Massachusetts, Sch Med, Dept Cell Biol, Worcester, MA 01605 USA; Millennium Pharmaceut Inc, Cambridge, MA USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (MAY 2001) Vol. 82, No. 1, pp. 110-122.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012 USA.
ISSN: 0730-2312.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 44
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

L8 ANSWER 10 OF 14 WPIDS (C) 2003 THOMSON DERWENT

TI Use of a proteasome inhibitor for reversing **proliferation** or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.

AN 2002-507279 [54] WPIDS

CR 1999-313169 [26]

AB US2002049157 A UPAB: 20020823

NOVELTY - A novel method for reversing an ongoing **proliferation** or activity, or both, of activated blood cells, comprises administering a proteasome inhibitor to an individual.

ACTIVITY - Immunosuppressive; Antiinflammatory; Antibacterial; Cytostatic.

MECHANISM OF ACTION - Proteasome inhibitor; inhibitors of CDK2 and Cyclin E.

The role of proteasome in T cell activation and **proliferation** was first examined in PBMC, using the proteasome-specific inhibitor LAC. The peripheral blood mononuclear cells (PBMC) were activated with various stimulants. LAC was added to the cells in the beginning of the culture (0 hours) along with the stimulants. 3H-thymidine uptake between 48 and 64 hours of 64 hour cultures was used as a parameter for cell **proliferation**. LAC strongly and dose-dependently inhibited the T cell **proliferation** induced by a T cell mitogen PHA by crosslinking TCR with anti-CD3 E, or by Ca++ ionophore plus cross-linking of the T cell co-stimulating molecule CD28. The T-cell-independent B cell **proliferation** induced with SAC plus IL-2 in tonsillar B cells was also potently inhibited by LAC. In all systems used, LAC at 5 micro M could exert near-to-maximal **inhibition**. The results suggest that LACs effect is not lymphocyte type (T or B cells)-specific nor stimulant-specific. It likely affects certain down-stream events governing a more general process in lymphocyte activation and **proliferation**

.

USE - The methods can be used for treating an adverse immune response such as an autoimmune disease or a graft rejection, or inflammation or septic shock (claimed). The methods can be used for reversing an ongoing **proliferation** or activity which may result in activated blood cells apoptosis, or **inhibition** of energy and oxygen supply to the activated blood cells, or where the **inhibition** of energy and oxygen supply is caused by disrupting mitochondrial function in activated blood cells or disruption of nitric acid synthesis (claimed). The methods can also be used for treating e.g. cancers, hyperthyroidisn and graft rejection.

The use of **DPBA** in organ transplantation-islet graft in streptozocin-induced diabetes in mice was studied. Islets from Balb/c mice in diabetic C57BL/6 recipients were used. The islets from syngeneic mice (isograft control) restored normal glycemia in diabetic mice, and the effect lasted more than 60 days as expected. The allogenic islets were rejected in about 10 days in untreated mice, and the mice became diabetic after an initial dip of their blood sugar level (allograft control). When the allogenic islets were transplanted to diabetic recipients along with **DPBA** treatment, the graft functioned normally beyond 60 days, indicating that the graft rejection was inhibited. This result showed that proteasome inhibitors as exemplified by **DPBA** can be used in human islet transplantation to prevent graft rejection. It was shown that a proteasome inhibitor such as **DPBA** inhibits the glucose elevation consequent to islet rejection.

ADVANTAGE - The proteasome inhibitors such as LAC and **DPBA** have shown an unique capacity to reverse an ongoing activity of blood cells. This reversal makes the possibility of treatment which selectively targets activated blood cells. The protease inhibitor are responsible for preventing allograft rejection for the first time successfully. Also an effective screening method for searching for other proteasome inhibitors has been found.

Dwg.0/31

ACCESSION NUMBER: 2002-507279 [54] WPIDS

CROSS REFERENCE: 1999-313169 [26]

DOC. NO. CPI: C2002-144189
TITLE: Use of a proteasome inhibitor for reversing **proliferation** or activity of activated blood cells for treating cancer, inflammation, autoimmune disease, graft rejection and septic shock.
DERWENT CLASS: B04 B05
INVENTOR(S): WANG, X; WU, J
PATENT ASSIGNEE(S): (WANG-I) WANG X; (WUJJ-I) WU J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002049157	A1	20020425	(200254)*		54

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2002049157	A1	CIP of	WO 1998-CA1010	19981029
		CIP of	US 1999-341009	19990825
		Provisional	US 2000-218145P	20000714
			US 2001-904251	20010712

PRIORITY APPLN. INFO: US 2000-218145P 20000714; WO 1998-CA1010 19981029; US 1999-341009 19990825; US 2001-904251 20010712

L8 ANSWER 11 OF 14 WPIDS (C) 2003 THOMSON DERWENT
TI **Inhibition** of mononuclear and T-cell production and development, especially in autoimmune diseases, comprises administration of inhibitor combination based on dipeptidyl-peptidase IV inhibitor.
AN 2002-114262 [15] WPIDS
AB WO 200189569 A UPAB: 20020306
NOVELTY - Dipeptidyl-peptidase IV inhibitors (I) are used in combination with alanyl-aminopeptidase inhibitors (II), X-Pro-aminopeptidase inhibitors (III), ACE inhibitors (IV) and/or prolyl-oligopeptidase inhibitors (V) to inhibit the activation, DNA synthesis and **proliferation** of human T-lymphocytes and mononuclear cells.
DETAILED DESCRIPTION - Inhibitors of enzymes with the same substrate specificity as dipeptidyl-peptidases IV and alanyl-aminopeptidases are included within inhibitors (I) and (II), respectively.
An INDEPENDENT CLAIM is also included for pharmaceutical preparations containing the combination of inhibitors with carriers, additives and/or adjuvants.
ACTIVITY - Immunosuppressive; antirheumatic; antiarthritic; dermatological; neuroprotective; antiinflammatory; antiulcer; antipsoriatic; nephrotropic; antianemic; antiarteriosclerotic; cytostatic.
MECHANISM OF ACTION - Enzyme inhibitor.
USE - The inhibitor combinations are useful for the prevention and treatment of autoimmune diseases, preferably rheumatoid arthritis, lupus erythematosus, multiple sclerosis, Crohn's disease, ulcerative colitis, psoriasis, neurodermatitis, glomerulonephritis, interstitial nephritis, vasculitis, autoimmune thyroid gland disorders, autoimmune haemolytic anemia, allergies with inflammatory origin and arteriosclerosis. They are also useful in suppressing transplant rejections and in the treatment of tumors.
ADVANTAGE - The combinations have a synergistic effect.
Dwg.0/0
ACCESSION NUMBER: 2002-114262 [15] WPIDS
DOC. NO. CPI: C2002-035017
TITLE: **Inhibition** of mononuclear and T-cell production and development, especially in autoimmune diseases,

comprises administration of inhibitor combination based on dipeptidyl-peptidase IV inhibitor.

DERWENT CLASS: B05

INVENTOR(S): ANSORGE, S; ARNDT, M; BUEHLING, F; LENDECKEL, U; NEUBERT, K; REINHOLD, D; BROCKE, S

PATENT ASSIGNEE(S): (MEDI-N) INST MEDIZINTECHNOLOGIE MAGDEBURG GMBH

COUNTRY COUNT: 96

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001089569	A1	20011129	(200215)*	GE	24
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
DE 10025464	A1	20011206	(200215)		
AU 2001067475	A	20011203	(200221)		
EP 1289559	A1	20030312	(200320)	GE	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001089569	A1	WO 2001-EP5887	20010522
DE 10025464	A1	DE 2000-10025464	20000523
AU 2001067475	A	AU 2001-67475	20010522
EP 1289559	A1	EP 2001-945184	20010522
		WO 2001-EP5887	20010522

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001067475	A	Based on	WO 200189569
EP 1289559	A1	Based on	WO 200189569

PRIORITY APPLN. INFO: DE 2000-10025464 20000523

L8 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.

TI 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer.

AB The 26S proteasome degrades proteins that regulate transcription factor activation, cell cycle progression, and apoptosis. In cancer, this may allow for uncontrolled cell division, promoting tumor growth, and spread. We examined whether selective **inhibition** of the 26S proteasome with PS-341, a **dipeptide boronic acid** analogue, would block **proliferation** and induce apoptosis in human pancreatic cancer. Proteasome **inhibition** significantly blocked mitogen (FCS) induced **proliferation** of BxPC3 human pancreatic cancer cells in vitro, while arresting cell cycle progression and inducing apoptosis by 24 h. Accumulation of p21Cip1-Waf-1, a cyclin dependent kinase (CDK) inhibitor normally degraded by the 26S proteasome, occurred by 3 h and correlated with cell cycle arrest. When BxPC3 pancreatic cancer xenografts were established in athymic nu/nu mice, weekly administration of 1 mg/kg PS-341 significantly inhibited tumor growth. Both cellular apoptosis and p21Cip1-Waf-1 protein levels were increased in PS-341 treated xenografts. **Inhibition** of tumor xenograft growth was greatest (89%) when PS-341 was combined with the tumoricidal agent CPT-11. Combined CPT-11/PS-341 therapy, but not single

agent therapy, yielded highly apoptotic tumors, significantly inhibited tumor cell **proliferation**, and blocked NF-kappaB activation indicating this systemic therapy was effective at the cancer cell level. 26S proteasome **inhibition** may represent a new therapeutic approach against this highly resistant and lethal malignancy.

ACCESSION NUMBER: 2001:309254 BIOSIS
DOCUMENT NUMBER: PREV200100309254
TITLE: 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer.
AUTHOR(S): Shah, Shimul A.; Potter, Michael W.; McDade, Theodore P.; Ricciardi, Rocco; Perugini, Richard A.; Elliott, Peter J.; Adams, Julian; Callery, Mark P. (1)
CORPORATE SOURCE: (1) University of Massachusetts Medical School, 55 Lake Avenue North, Worcester, MA, 01655: callerym@ummhc.org USA
SOURCE: Journal of Cellular Biochemistry, (2 April 27 April) Vol. 82, No. 1, pp. 110-122. print.
ISSN: 0730-2312.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L8 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2003 ACS
TI Mechanisms of Proteasome Inhibitor PS-341-induced G2-M-Phase Arrest and Apoptosis in Human Non-Small Cell Lung Cancer Cell Lines
AB PURPOSE: PS-341 is a novel **dipeptide boronic acid** proteasome inhibitor with in vitro and in vivo antitumor activity that induces mechanisms of apoptosis by unknown mechanisms. Exptl. Design: Human non-small cell lung cancer cell lines were used to investigate effects PS-341 on cell **proliferation**, cell cycle progression, and the induction of apoptosis. RESULTS: PS-341 was 38-360-fold more cytotoxic against H460 cells when compared with the proteasome inhibitors MG-132 and PSI. Differential PS-341 cytotoxic effects were found with respect to P53 function: H322 cells (p53 mutant) were 6-fold less sensitive as compared with H460 cells (p53 wild type); and H358 cells (p53 null) were 1.6-fold more sensitive as compared with H460 cells (p53 wild type). A concn.- and time-dependent cell cycle blockade at G2-M phase was seen for H460 cells without any direct effects on microtubule polymn. or depolymn. PS-341 exposure in H460 cells led to stabilization of p53, induction of p21cip/waf-1 and MDM2 expression, an increase in cyclin B and cyclin A, and the activation of cyclin B and cyclin A kinases. MDM2 induction was found only in H460 cells, whereas in H322 and H358 cells, G2-M-phase arrest, p21cip/waf-1 induction, and an increase in cyclin B1 were found. The commitment of G2-M-phase cells to apoptosis was verified by the activation of caspase-3 and cleavage of poly(ADP-ribose) polymerase in drug-free medium. CONCLUSIONS: Our data suggest that the PS-341-induced G2-M-phase arrest may be assocd. with the **inhibition** of degrdn. of cell cycle regulators and that the up-regulation of p21cip/waf-1 expression may be via p53-dependent and/or -independent pathways. The resulting disturbance of cell cycle progression leads either to growth **inhibition** or to the initiation of apoptotic pathways.

ACCESSION NUMBER: 2003:196175 HCAPLUS
TITLE: Mechanisms of Proteasome Inhibitor PS-341-induced G2-M-Phase Arrest and Apoptosis in Human Non-Small Cell Lung Cancer Cell Lines
AUTHOR(S): Ling, Yi-He; Liebes, Leonard; Jiang, Jian-Dong; Holland, James F.; Elliott, Peter J.; Adams, Julian; Muggia, Franco M.; Perez-Soler, Roman
CORPORATE SOURCE: Department of Oncology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA
SOURCE: Clinical Cancer Research (2003), 9(3), 1145-1154
CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal

LANGUAGE: English
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2003 ACS
TI 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer
AB The 26S proteasome degrades proteins that regulate transcription factor activation, cell cycle progression, and apoptosis. In cancer, this may allow for uncontrolled cell division, promoting tumor growth, and spread. We examd. whether selective **inhibition** of the 26S proteasome with PS-341, a **dipeptide boronic acid** analog, would block **proliferation** and induce apoptosis in human pancreatic cancer. Proteasome **inhibition** significantly blocked mitogen (FCS) induced **proliferation** of BxPC3 human pancreatic cancer cells in vitro, while arresting cell cycle progression and inducing apoptosis by 24 h. Accumulation of p21Cip1-Waf-1, a cyclin dependent kinase (CDK) inhibitor normally degraded by the 26S proteasome, occurred by 3 h and correlated with cell cycle arrest. When BxPC3 pancreatic cancer xenografts were established in athymic nu/nu mice, weekly administration of 1 mg/kg PS-341 significantly inhibited tumor growth. Both cellular apoptosis and p21Cip1-Waf-1 protein levels were increased in PS-341 treated xenografts. **Inhibition** of tumor xenograft growth was greatest (89%) when PS-341 was combined with the tumoricidal agent CPT-11. Combined CPT-11/PS-341 therapy, but not single agent therapy, yielded highly apoptotic tumors, significantly inhibited tumor cell **proliferation**, and blocked NF-.kappa.B activation indicating this systemic therapy was effective at the cancer cell level. 26S proteasome **inhibition** may represent a new therapeutic approach against this highly resistant and lethal malignancy.
ACCESSION NUMBER: 2001:412094 HCAPLUS
DOCUMENT NUMBER: 135:174873
TITLE: 26S proteasome **inhibition** induces apoptosis and limits growth of human pancreatic cancer
AUTHOR(S): Shah, Shimul A.; Potter, Michael W.; McDade, Theodore P.; Ricciardi, Rocco; Perugini, Richard A.; Elliott, Peter J.; Adams, Julian; Callery, Mark P.
CORPORATE SOURCE: Department of Surgery, University of Massachusetts Medical School, Worcester, MA, 01655, USA
SOURCE: Journal of Cellular Biochemistry (2001), 82(1), 110-122
CODEN: JCEBD5; ISSN: 0730-2312
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 16:18:28 ON 23 JUN 2003)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, SCISEARCH, WPIDS, BIOSIS, FSTA, JICST-EPLUS, HCAPLUS, JAPIO' ENTERED AT 16:19:34 ON 23 JUN 2003

L1	3668	S	LACTACYSTIN
L2	243	S	DIPEPTIDE BORONIC ACID OR DPBA
L3	4499	S	PROTEASOME INHIBITOR
L4	2	S	L3 AND ACTIVATED BLOOD CELLS
L5	281	S	L1 AND PROLIFERATION
L6	22	S	L2 AND PROLIFERATION
L7	3	S	L5 AND L6
L8	14	S	L6 AND INHIBITION
L9	176	S	L5 AND INHIBITION

=> d l9 ti abs ibib 1-15

L9 ANSWER 1 OF 176 MEDLINE
TI **Inhibition** of the proteasome by **lactacystin** enhances oligodendroglial cell differentiation.
AB We have used **lactacystin**, a specific inhibitor of the 26S proteasome, in oligodendroglial cell (OLGc) primary cultures to explore the possible participation of the proteasome-ubiquitin-dependent pathway in the decision of the OLGcs to arrest their **proliferation** and start differentiation. Addition of **lactacystin** at various concentrations to cultures containing a majority of OLGc was found to produce their withdrawal from the cell cycle and to induce their biochemical and morphological differentiation, with the appearance of extensive myelin-like sheets. The three classic proteolytic activities of the proteasome were significantly decreased in the **lactacystin** -treated cultures, and the immunocytochemical analysis showed an increase in the number of O4-, O1-, myelin basic protein-, and myelin proteolipid protein-positive cells and a decrease in A2B5-reacting cells. Quantitative immunochemical evaluation of the expression of certain proteins controlling the cell cycle showed an increase in p27kip1-, cyclin D-, and cdk4-positive cells, with a decrease in cyclin E- and cdk2-positive cells. In the **lactacystin**-treated OLGcs, there was a dose-dependent decrease in the number of cells incorporating bromodeoxyuridine and in the activity of the complexes cyclin D-cdk4 and cyclin E-cdk2. Furthermore, increased levels of expression of several STAT factors were found, suggesting that proteasome **inhibition** in OLGcs could stabilize signals of survival and differentiation that might be processed through the JAK/STAT signaling cascade.
ACCESSION NUMBER: 2003278043 IN-PROCESS
DOCUMENT NUMBER: 22689502 PubMed ID: 12805303
TITLE: **Inhibition** of the proteasome by **lactacystin** enhances oligodendroglial cell differentiation.
AUTHOR: Pasquini Laura A; Paez Pablo M; Moreno Marcos A N Besio; Pasquini Juana M; Soto Eduardo F
CORPORATE SOURCE: Departamento de Quimica Biologica, Instituto de Quimica y Fisicoquimica Biologica, Facultad de Farmacia y Bioquimica, Universidad de Buenos Aires, Consejo Nacional de Investigaciones Cientificas y Tecnicas, Buenos Aires 1113, Argentina.
SOURCE: JOURNAL OF NEUROSCIENCE, (2003 Jun 1) 23 (11) 4635-44. Journal code: 8102140. ISSN: 1529-2401.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20030614
Last Updated on STN: 20030614

L9 ANSWER 2 OF 176 MEDLINE
TI Cycling B-CLL cells are highly susceptible to **inhibition** of the proteasome: involvement of p27, early D-type cyclins, Bax, and caspase-dependent and -independent pathways.
AB OBJECTIVE: Although peripheral blood B-CLL cells are arrested in G0 phase of the cell cycle, a proliferating pool of cells in **proliferation** centers might be involved in disease progression. We have previously described an in vitro model of this proliferating pool of cells using B-CLL cells stimulated with immunostimulatory oligonucleotides (CpG-ODN) and interleukin-2. **Lactacystin** is a specific inhibitor of the proteasome and is a potent apoptosis inductor in resting peripheral B-CLL cells. In the present study, we investigated the effect of proteasome **inhibition** in proliferating B-CLL cells. METHODS: The effect of proteasome **inhibition** was analyzed using thymidine

incorporation, annexin V assays, and TUNEL staining. Immunoblots were performed to evaluate expression of proteins involved in cell cycle and apoptosis regulation. RESULTS: **Lactacystin** blocked cell cycle progression in activated B-CLL cells and inhibited degradation of p27. Upregulation of cyclin D2 and D3 in activated B-CLL cells was inhibited while the expression of cdk2, cdk4, and cyclin E remained unchanged. Activated B-CLL cells were more susceptible to apoptosis induction as compared to resting B-CLL cells. Apoptosis induction was accompanied by cleavage of Bax, procaspase 8, procaspase 9, and procaspase 3. However, a broad-spectrum caspase inhibitor (z-VAD.fmk) only partially inhibited cell death although DNA degradation was completely inhibited. CONCLUSION: Proteasome **inhibition** is highly effective in proliferating B-CLL cells and induces apoptosis using a caspase-dependent and -independent pathway.

ACCESSION NUMBER: 2003129933 MEDLINE
DOCUMENT NUMBER: 22531090 PubMed ID: 12644019
TITLE: Cycling B-CLL cells are highly susceptible to **inhibition** of the proteasome: involvement of p27, early D-type cyclins, Bax, and caspase-dependent and -independent pathways.
AUTHOR: Bogner Christian; Schneller Folker; Hipp Susanne; Ringshausen Ingo; Peschel Christian; Decker Thomas
CORPORATE SOURCE: IIIrd Department of Medicine, Technical University of Munich, Munich, Germany.
SOURCE: EXPERIMENTAL HEMATOLOGY, (2003 Mar) 31 (3) 218-25. Journal code: 0402313. ISSN: 0301-472X.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 20030320
Last Updated on STN: 20030513
Entered Medline: 20030509

L9 ANSWER 3 OF 176 MEDLINE
TI Curcumin-induced suppression of cell **proliferation** correlates with down-regulation of cyclin D1 expression and CDK4-mediated retinoblastoma protein phosphorylation.
AB Cyclin D1 is a proto-oncogene that is overexpressed in many cancers including breast and prostate. It plays a role in cell **proliferation** through activation of cyclin-dependent kinases. Curcumin, a diferuloylmethane, is a chemopreventive agent known to inhibit the **proliferation** of several breast and prostate cancer cell lines. It is possible that the effect of curcumin is mediated through the regulation of cyclin D1. In the present report we show that **inhibition** of the **proliferation** of various prostate, breast and squamous cell carcinoma cell lines by curcumin correlated with the down-regulation of the expression of cyclin D1 protein. In comparison, the down-regulation by curcumin of cyclin D2 and cyclin D3 was found only in selective cell lines. The suppression of cyclin D1 by curcumin led to **inhibition** of CDK4-mediated phosphorylation of retinoblastoma protein. We found that curcumin-induced down-regulation of cyclin D1 was inhibited by **lactacystin**, an inhibitor of 26S proteosome, suggesting that curcumin represses cyclin D1 expression by promoting proteolysis. We found that curcumin also down-regulated mRNA expression, thus suggesting transcriptional regulation. Curcumin also inhibited the activity of the cyclin D1 promoter-dependent reporter gene expression. Overall our results suggest that curcumin down-regulates cyclin D1 expression through activation of both transcriptional and post-transcriptional mechanisms, and this may contribute to the antiproliferative effects of curcumin against various cell types.
ACCESSION NUMBER: 2002721275 MEDLINE

DOCUMENT NUMBER: 22371573 PubMed ID: 12483537
TITLE: Curcumin-induced suppression of cell **proliferation** correlates with down-regulation of cyclin D1 expression and CDK4-mediated retinoblastoma protein phosphorylation.
AUTHOR: Mukhopadhyay Asok; Banerjee Sanjeev; Stafford Lewis Joe; Xia Chunzhi; Liu Mingyao; Aggarwal Bharat B
CORPORATE SOURCE: Cytokine Research Laboratory, Department of Bioimmunotherapy, The University of Texas MD Anderson Cancer Center, Box 143, 1515 Holcombe Boulevard, Houston, Texas, TX 77030, USA.
SOURCE: ONCOGENE, (2002 Dec 12) 21 (57) 8852-61.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 20021218
Last Updated on STN: 20030124
Entered Medline: 20030123

L9 ANSWER 4 OF 176 MEDLINE
TI Cleavage of p21waf1 by proteinase-3, a myeloid-specific serine protease, potentiates cell **proliferation**.
AB In this study, we present evidence for the critical role of proteinase-3 (PR3) in the **proliferation** of myeloid cells via the proteolytic regulation of the cyclin-dependent kinase inhibitor p21(waf1). Expression of recombinant PR3 in rat (RBL) or human (HMC1) mast cell lines increased bromodeoxyuridine incorporation and CDK2 activity compared with RBL and HMC1 cells transfected with an enzymatically inactive PR3 mutant (PR3(S203A)) or with human neutrophil elastase. Western blot analysis of p21(waf1) showed an absence of detectable protein, despite normal levels of p21 mRNA. Ectopic overexpression of p21 restored normal levels of p21 in the RBL/PR3/p21 double transfectants and reverted the proliferative effect of PR3. **Inhibition** of the 26 S proteasome by **lactacystin** or of caspases by benzyloxycarbonyl-Val-Ala-Asp-fluoromethyl ketone did not inhibit p21 proteolysis. p21 cleavage correlated with PR3 expression in HMC1 cells infected with recombinant adenoviral vector Ad/PR3. During in vitro studies, purified p21 was cleaved by PR3, resulting in a 10-kDa p21 fragment. Employing double immunofluorescence confocal microscopy, subcellular fractionation, and co-immunoprecipitation, we found that PR3 and p21 colocalized in the cytosol. In human neutrophils treated with tumor necrosis factor-alpha, which induces PR3 re-expression, we observed that p21 disappeared and was reversed by Pefabloc, a serine proteinase inhibitor. The physiopathological implications of the cleavage of p21 by PR3 have to be determined.
ACCESSION NUMBER: 2002696046 MEDLINE
DOCUMENT NUMBER: 22344669 PubMed ID: 12354776
TITLE: Cleavage of p21waf1 by proteinase-3, a myeloid-specific serine protease, potentiates cell **proliferation**.
AUTHOR: Witko-Sarsat Veronique; Canteloup Sandrine; Durant Stephanie; Desdouets Chantal; Chabernaud Romain; Lemarchand Patricia; Descamps-Latscha Beatrice
CORPORATE SOURCE: INSERM U507, Hopital Necker, 161, rue de Sevres, and INSERM U370, Faculte de Medecine Necker, 156 rue de Vaugirard, 75015 Paris, France and INSERM U533, Faculte de Medecine, 1 rue Gaston Veil, 44000 Nantes, France.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2002 Dec 6) 277 (49) 47338-47.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: Priority Journals
ENTRY MONTH: 200302
ENTRY DATE: Entered STN: 20021217
Last Updated on STN: 20030205
Entered Medline: 20030204

L9 ANSWER 5 OF 176 MEDLINE
TI Proteasome **inhibition** reduces superantigen-mediated T cell activation and the severity of psoriasis in a SCID-hu model.
AB There is increasing evidence that bacterial superantigens contribute to inflammation and T cell responses in psoriasis. Psoriatic inflammation entails a complex series of inductive and effector processes that require the regulated expression of various proinflammatory genes, many of which require NF-kappa B for maximal trans-activation. PS-519 is a potent and selective proteasome inhibitor based upon the naturally occurring compound **lactacystin**, which inhibits NF-kappa B activation by blocking the degradation of its inhibitory protein I kappa B. We report that proteasome **inhibition** by PS-519 reduces superantigen-mediated T cell-activation in vitro and in vivo. **Proliferation** was inhibited along with the expression of very early (CD69), early (CD25), and late T cell (HLA-DR) activation molecules. Moreover, expression of E-selectin ligands relevant to dermal T cell homing was reduced, as was E-selectin binding in vitro. Finally, PS-519 proved to be therapeutically effective in a SCID-hu xenogeneic psoriasis transplantation model. We conclude that **inhibition** of the proteasome, e.g., by PS-519, is a promising means to treat T cell-mediated disorders such as psoriasis.
ACCESSION NUMBER: 2002145486 MEDLINE
DOCUMENT NUMBER: 21866499 PubMed ID: 11877475
TITLE: Proteasome **inhibition** reduces superantigen-mediated T cell activation and the severity of psoriasis in a SCID-hu model.
AUTHOR: Zollner Thomas M; Podda Maurizio; Pien Christine; Elliott Peter J; Kaufmann Roland; Boehncke Wolf-Henning
CORPORATE SOURCE: Department of Dermatology, J.W. Goethe University of Frankfurt, Frankfurt, Germany.. Thomas.Zollner@Schering.de
SOURCE: JOURNAL OF CLINICAL INVESTIGATION, (2002 Mar) 109 (5) 671-9.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200204
ENTRY DATE: Entered STN: 20020307
Last Updated on STN: 20020404
Entered Medline: 20020403

L9 ANSWER 6 OF 176 MEDLINE
TI Proteasome activity is required for T lymphocyte aggregation after mitogen activation.
AB The proteasome is a multicatalytic complex of proteases involved in T lymphocyte **proliferation** and activation through multiple mechanisms. In this study, we investigated its role in lymphocyte aggregation. We found that blocking proteasome activity by a proteasome-specific inhibitor **lactacystin** (LAC) prevented clustering of T lymphocytes after stimulation with various mitogens. Expression of adhesion molecules ICAM-1 and LFA-1 at cell surfaces of activated T cells was decreased after treatment with LAC. Mechanisms by which the proteasome intervenes in the expression of these adhesion molecules were different. LAC inhibited ICAM-1 expression at the mRNA level, whereas LFA-1 **inhibition** was probably at a post-translational level. Downregulation of these molecules after proteasome **inhibition** likely contributes to the observed repression of T cell aggregation. Our results show that the proteasome

plays an important role in cell-cell interaction during T cell activation. Copyright 2001 Wiley-Liss, Inc.

ACCESSION NUMBER: 2001435616 MEDLINE
DOCUMENT NUMBER: 21135931 PubMed ID: 11241674
TITLE: Proteasome activity is required for T lymphocyte aggregation after mitogen activation.
AUTHOR: Kanaan N; Luo H; Wu J
CORPORATE SOURCE: Research Center, Notre-Dame Hospital, CHUM, University of Montreal, Montreal, Canada.
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (2001 Mar 26) 81 (2) 347-56.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010806
Last Updated on STN: 20010806
Entered Medline: 20010802

L9 ANSWER 7 OF 176 MEDLINE
TI Rapid induction of histone hyperacetylation and cellular differentiation in human breast tumor cell lines following degradation of histone deacetylase-1.
AB Quinidine inhibits **proliferation** and promotes cellular differentiation in human breast tumor epithelial cells. Previously we showed quinidine arrested MCF-7 cells in G(1) phase of the cell cycle and led to a G(1) to G(0) transition followed by apoptotic cell death. The present experiments demonstrated that MCF-7, MCF-7ras, T47D, MDA-MB-231, and MDA-MB-435 cells transiently differentiate before undergoing apoptosis in response to quinidine. The cells accumulated lipid droplets, and the cytokeratin 18 cytoskeleton was reorganized. Hyperacetylated histone H4 appeared within 2 h of the addition of quinidine to the medium, and levels were maximal by 24 h. Quinidine-treated MCF-7 cells showed elevated p21(WAF1), hypophosphorylation and suppression of retinoblastoma protein, and down-regulation of cyclin D1, similar to the cell cycle response observed with cells induced to differentiate by histone deacetylase inhibitors, trichostatin A, and trapoxin. Quinidine did not show evidence for direct **inhibition** of histone deacetylase enzymatic activity in vitro. HDAC1 was undetectable in MCF-7 cells 30 min after addition of quinidine to the growth medium. The proteasome inhibitors MG-132 and **lactacystin** completely protected HDAC1 from the action of quinidine. We conclude that quinidine is a breast tumor cell differentiating agent that causes the loss of HDAC1 via a proteasomal sensitive mechanism.

ACCESSION NUMBER: 2001069352 MEDLINE
DOCUMENT NUMBER: 20519620 PubMed ID: 10938272
TITLE: Rapid induction of histone hyperacetylation and cellular differentiation in human breast tumor cell lines following degradation of histone deacetylase-1.
AUTHOR: Zhou Q; Melkoumian Z K; Lucktong A; Moniwa M; Davie J R; Strobl J S
CORPORATE SOURCE: Department of Pharmacology & Toxicology, Robert C. Byrd Health Sciences Center, West Virginia University, Morgantown, West Virginia 26506, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Nov 10) 275 (45) 35256-63.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104

L9 ANSWER 8 OF 176 MEDLINE
TI Proteasome inhibitor induced gene expression profiles reveal overexpression of transcriptional regulators ATF3, GADD153 and MAD1.
AB The ubiquitin/proteasome pathway has been implicated in a wide variety of cellular processes and the number of substrates degraded by the proteasome is impressive. Most prominently, the stability of a large number of transcription factors is regulated by ubiquitination. To elucidate pathways regulated by the proteasome, gene expression profiles were generated, comparing changes of mRNA expression of 7900 genes from the UniGene collection upon exposure of cells to the proteasome inhibitors **Lactacystin**, **Lactacystin**-beta-lactone or MG132 by means of microarray based cDNA hybridization. The three profiles were very similar, but differed significantly from a gene expression profile generated with the histone deacetylase inhibitor Trapoxin A, indicating that the observed alterations were indeed due to proteasome **inhibition**. Two of the most prominently induced genes encoded the growth arrest and DNA damage inducible protein Gadd153 and the activating transcription factor ATF3, both transcription factors of the CCAAT/enhancer binding protein (C/EBP) family. A third gene encoded for the transcriptional repressor and c-Myc antagonist Mad1. Our results suggest that proteasome **inhibition** leads to upregulation of specific members of transcription factor families controlling cellular stress response and **proliferation**. Oncogene (2000).
ACCESSION NUMBER: 2000332399 MEDLINE
DOCUMENT NUMBER: 20332399 PubMed ID: 10871842
TITLE: Proteasome inhibitor induced gene expression profiles reveal overexpression of transcriptional regulators ATF3, GADD153 and MAD1.
AUTHOR: Zimmermann J; Erdmann D; Lalande I; Grossenbacher R; Noorani M; Furst P
CORPORATE SOURCE: Novartis Pharma AG, Oncology Research, WKL-125.13.14, CH-4002 Basel, Switzerland.
SOURCE: ONCOGENE, (2000 Jun 8) 19 (25) 2913-20.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000720
Last Updated on STN: 20000720
Entered Medline: 20000712

L9 ANSWER 9 OF 176 MEDLINE
TI The selective proteasome inhibitors **lactacystin** and epoxomicin can be used to either up- or down-regulate antigen presentation at nontoxic doses.
AB The complete **inhibition** of proteasome activities interferes with the production of most MHC class I peptide ligands as well as with cellular **proliferation** and survival. In this study we have investigated how partial and selective **inhibition** of the chymotrypsin-like activity of the proteasome by the proteasome inhibitors **lactacystin** or epoxomicin would affect Ag presentation. At 0.5-1 microM **lactacystin**, the presentation of the lymphocytic choriomeningitis virus-derived epitopes NP118 and GP33 and the mouse CMV epitope pp89-168 were reduced and were further diminished in a dose-dependent manner with increasing concentrations. Presentation of the lymphocytic choriomeningitis virus-derived epitope GP276, in contrast, was markedly enhanced at low, but abrogated at higher, concentrations of either **lactacystin** or epoxomicin. The inhibitor-mediated

effects were thus epitope specific and did not correlate with the degradation rates of the involved viral proteins. Although neither apoptosis induction nor interference with cellular **proliferation** was observed at 0.5-1 microM **lactacystin** in vivo, this concentration was sufficient to alter the fragmentation of polypeptides by the 20S proteasome in vitro. Our results indicate that partial and selective **inhibition** of proteasome activity in vivo is a valid approach to modulate Ag presentation, with potential applications for the treatment of autoimmune diseases and the prevention of transplant rejection.

ACCESSION NUMBER: 2000302761 MEDLINE
DOCUMENT NUMBER: 20302761 PubMed ID: 10843664
TITLE: The selective proteasome inhibitors **lactacystin** and epoxomicin can be used to either up- or down-regulate antigen presentation at nontoxic doses.
AUTHOR: Schwarz K; de Giuli R; Schmidtke G; Kostka S; van den Broek M; Kim K B; Crews C M; Kraft R; Groettrup M
CORPORATE SOURCE: Research Department, Cantonal Hospital St. Gall, St. Gallen, Switzerland.
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Jun 15) 164 (12) 6147-57. Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000728
Last Updated on STN: 20021210
Entered Medline: 20000720

L9 ANSWER 10 OF 176 MEDLINE
TI Effects of geldanamycin, a heat-shock protein 90-binding agent, on T cell function and T cell nonreceptor protein tyrosine kinases.
AB The benzoquinoid ansamycins geldanamycin (GA), herbimycin, and their derivatives are emerging as novel therapeutic agents that act by inhibiting the 90-kDa heat-shock protein hsp90. We report that GA inhibits the **proliferation** of mitogen-activated T cells. GA is actively toxic to both resting and activated T cells; activated T cells appear to be especially vulnerable. The mechanism by which GA acts is reflected by its effects on an essential hsp90-dependent protein, the T cell-specific nonreceptor tyrosine kinase lck. GA treatment depletes lck levels in cultured T cells by a kinetically slow dose-dependent process. Pulse-chase analyses indicate that GA induces the very rapid degradation of newly synthesized lck molecules. GA also induces a slower degradation of mature lck populations. These results correlate with global losses in protein tyrosine kinase activity and an inability to respond to TCR stimuli, but the activity of mature lck is not immediately compromised. Although the specific proteasome inhibitor **lactacystin** provides marginal protection against GA-induced lck depletion, proteasome **inhibition** also induces changes in lck detergent solubility independent of GA application. There is no other evidence for the involvement of the proteosome. Lysosome **inhibition** provides quantitatively superior protection against degradation. These results indicate that pharmacologic **inhibition** of hsp90 chaperone function may represent a novel immunosuppressant strategy, and elaborate on the appropriate context in which to interpret losses of lck as a reporter for the pharmacology of GA in whole organisms.

ACCESSION NUMBER: 2000171487 MEDLINE
DOCUMENT NUMBER: 20171487 PubMed ID: 10706677
TITLE: Effects of geldanamycin, a heat-shock protein 90-binding agent, on T cell function and T cell nonreceptor protein tyrosine kinases.
AUTHOR: Yorgin P D; Hartson S D; Fellah A M; Scroggins B T; Huang W; Katsanis E; Couchman J M; Matts R L; Whitesell L

CORPORATE SOURCE: Department of Pediatrics, Steele Memorial Children's Research Center, University of Arizona, Tucson, AZ 85724, USA.. pyorgin@stanford.edu
CONTRACT NUMBER: CA59537 (NCI)
GM51608 (NIGMS)
SOURCE: JOURNAL OF IMMUNOLOGY, (2000 Mar 15) 164 (6) 2915-23.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000328

L9 ANSWER 11 OF 176 MEDLINE
TI The proteasome controls the expression of a **proliferation**-associated nuclear antigen Ki-67.
AB The proteasome is a protease complex responsible for rapid, selective, and irreversible removal of regulatory proteins, as well as many other cellular proteins. In this study, we have demonstrated that a **proliferation**-associated nuclear protein Ki-67 depended on the proteasome for its rapid degradation. A proteasome-specific inhibitor **lactacystin** augmented Ki-67 protein levels in pancreatic cancer BxPC-3 cells while repressed the level of steady-state Ki-67 mRNA. **Inhibition** of the proteasome also led to accumulation of two CDK inhibitors p27(kip1) and p21(cip1) in the BxPC-3 cells. Failed reduction of Ki-67 protein and enhanced levels of the two CDK inhibitors are likely contributing factors for the suppressed BxPC-3 **proliferation** after proteasome **inhibition**.

ACCESSION NUMBER: 2000120818 MEDLINE
DOCUMENT NUMBER: 20120818 PubMed ID: 10653979
TITLE: The proteasome controls the expression of a **proliferation**-associated nuclear antigen Ki-67.
AUTHOR: Wu Y; Luo H; Kanaan N; Wu J
CORPORATE SOURCE: Department of Surgery, Second Affiliated Hospital of Zhejiang Medical College, Zhejiang University, Hangzhou, China.
SOURCE: JOURNAL OF CELLULAR BIOCHEMISTRY, (2000 Jan) 76 (4) 596-604.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000320
Last Updated on STN: 20000320
Entered Medline: 20000309

L9 ANSWER 12 OF 176 MEDLINE
TI Delayed and sustained activation of p42/p44 mitogen-activated protein kinase induced by proteasome inhibitors through p21(ras) in PC12 cells.
AB Proteolysis by the ubiquitin/proteasome pathway regulates the intracellular level of several proteins, some of which control cell **proliferation** and cell cycle progression. To determine what kinds of signaling cascades are activated or inhibited by proteasome **inhibition**, we treated PC12 cells with specific proteasome inhibitors and subsequently performed in-gel kinase assays. N-Acetyl-Leu-Leu-norleucinal and **lactacystin**, which inhibit the activity of the proteasome, induced the activation of p42/p44 mitogen-activated protein (MAP) kinases [extracellular signal-regulated

kinases (ERKs) 1 and 2]. In contrast, N-acetyl-Leu-Leu-methional, which inhibits the activity of calpains, but not of the proteasome, failed to induce ERK activation. Uniquely, the kinetics of MAP kinase activation induced by proteasome inhibitors are very slow compared with those resulting from activation by nerve growth factor; ERK activation is detectable only after a 5-h treatment with the inhibitors, and its activity remained unchanged for at least until 27 h. Proteasome inhibitor-initiated ERK activation is inhibited by pretreatment with the ERK kinase inhibitor PD 98059, as well as by overexpression of a dominant-negative form of Ras. Thus, proteasome inhibitors induce sustained ERK activation in a Ras-dependent manner. Proteasome inhibitor-induced neurite outgrowth, however, is not inhibited by PD 98059, indicating that sustained activation of ERKs is not the factor responsible for proteasome inhibitor-induced morphological differentiation. Our data suggest the presence of a novel mechanism for activation of the MAP kinase cascade that involves proteasome activity.

ACCESSION NUMBER: 2000083399 MEDLINE
DOCUMENT NUMBER: 20083399 PubMed ID: 10617109
TITLE: Delayed and sustained activation of p42/p44 mitogen-activated protein kinase induced by proteasome inhibitors through p21(ras) in PC12 cells.
AUTHOR: Hashimoto K; Guroff G; Katagiri Y
CORPORATE SOURCE: Section on Growth Factors, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892, USA.
SOURCE: JOURNAL OF NEUROCHEMISTRY, (2000 Jan) 74 (1) 92-8. Journal code: 2985190R. ISSN: 0022-3042.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000118

L9 ANSWER 13 OF 176 MEDLINE
TI Regulation of BRCA1 by protein degradation.
AB BRCA1, a tumor suppressor protein implicated in hereditary forms of breast and ovarian cancer, is transcriptionally regulated in a **proliferation**-dependent manner. In this study, we demonstrate a substantial role for proteolysis in regulating the BRCA1 steady-state protein level in several cell lines. N-acetyl-leu-leu-norleucinal (ALLN), an inhibitor of the proteasome, calpain, and cathepsins, caused BRCA1 protein to accumulate in the nucleus of several human breast, prostate, and melanoma cell lines which express low or undetectable basal levels of BRCA1 protein, but not in cells with high basal expression of BRCA1. Protease **inhibition** did not increase BRCA1 synthesis, nor change its mRNA level, but it dramatically prolonged the protein's half-life. In contrast to ALLN, **lactacystin** and PS341, two specific proteasome inhibitors, as well as calpastatin peptide and PD150606, two selective calpain inhibitors, had no effect on BRCA1 stability, whereas ALLM, an effective calpain and cathepsin inhibitor but weak proteasome inhibitor, did stimulate accumulation of BRCA1. Moreover, three inhibitors of acidic cysteine proteases, chloroquine, ammonium chloride and bafilomycin, were as effective as ALLN. These results demonstrate that degradation by a cathepsin-like protease in fine balance with BRCA1 transcription is responsible for maintaining the low steady-state level of BRCA1 protein seen in many cancer cells.

ACCESSION NUMBER: 2000065116 MEDLINE
DOCUMENT NUMBER: 20065116 PubMed ID: 10597248
TITLE: Regulation of BRCA1 by protein degradation.
AUTHOR: Blagosklonny M V; An W G; Melillo G; Nguyen P; Trepel J B; Neckers L M

CORPORATE SOURCE: Department of Therapeutics, National Cancer Institute, NIH, Bethesda, Maryland, MD 20892, USA.
SOURCE: ONCOGENE, (1999 Nov 11) 18 (47) 6460-8.
Journal code: 8711562. ISSN: 0950-9232.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000114
Last Updated on STN: 20000114
Entered Medline: 20000104

L9 ANSWER 14 OF 176 MEDLINE
TI Role of proteasomes in T cell activation and **proliferation**.
AB The role of proteasomes in T cell activation, **proliferation**, and apoptosis was investigated using a proteasome-specific inhibitor **lactacystin** (LAC). **Inhibition** of the proteasome activity by LAC repressed the mitogen-induced T cell **proliferation**. The proteasome activity was definitively required for the T cells to progress from the G0 to S phase. It was necessary to optimize the progress from the G1/S boundary to the G2/M phase, but not for the progress from the G2/M phase to the next G1 phase. Probably as a result of a blockage of cell cycle progress, the cycling, but not the resting, T cells underwent apoptosis when treated with LAC. Mechanistically, we have found that cyclin-dependent kinase-2 (CDK2) and the cyclin E-associated kinase (largely CDK2), but not CDK4, in the G1 phase were strongly inhibited by LAC. This could be an important mechanism for the proteasome to regulate the cell cycle. The degradation of cyclin E in the late G1 and early S phases was dependent on the proteasome, although it was unlikely that this accounted for the observed **inhibition** of T cell **proliferation**. There was a reduced decay of p27Kip1 in the late G1 phase when the proteasome activity was suppressed, and this might be a contributing mechanism for the observed **inhibition** of CDK2 activity. Interestingly, p21Cip1 was up-regulated during the G1 phase, and the up-regulation was inhibited by LAC. Our study shows that the proteasome plays pivotal roles in regulating T cell activation and **proliferation**, and its effect is probably exerted through multiple mechanisms.
ACCESSION NUMBER: 1998211640 MEDLINE
DOCUMENT NUMBER: 98211640 PubMed ID: 9551914
TITLE: Role of proteasomes in T cell activation and **proliferation**.
AUTHOR: Wang X; Luo H; Chen H; Duguid W; Wu J
CORPORATE SOURCE: Louis-Charles Simard Research Center, Notre-Dame Hospital, University of Montreal, Quebec, Canada.
SOURCE: JOURNAL OF IMMUNOLOGY, (1998 Jan 15) 160 (2) 788-801.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980507
Last Updated on STN: 20000303
Entered Medline: 19980430

Considered

L9 ANSWER 15 OF 176 MEDLINE
TI **Inhibition** of proteasome activity blocks cell cycle progression at specific phase boundaries in African trypanosomes.
AB Proteasomes are one of the cellular complexes controlling protein degradation from archaebacteria to mammalian cells. We recently purified and characterized the catalytic core of the proteasome, the 20S form, from Trypanosoma brucei, a flagellated protozoa which causes African

trypanosomiasis. To identify the role of proteasomes in African trypanosomes, we used **lactacystin**, a specific inhibitor of proteasome activity. **Lactacystin** showed potent **inhibition** of the activity of 20S proteasomes purified from both bloodstream and procyclic (insect) forms of T. brucei (IC50 = 1 microM). It also inhibited **proliferation** of T. brucei cells in culture assays, with 1 microM inhibiting growth of bloodstream forms, whereas 5 microM was required to block **proliferation** of procyclic forms. Analysis of the DNA content of these cells by flow cytometry showed that 5 microM **lactacystin** arrested procyclic cells in the G2 + M phases of the cell cycle. Fluorescence microscopy revealed that most of the cells had one nucleus and one kinetoplast each, indicating that the cells had replicated their DNA, but failed to undergo mitosis. This suggests that transition from G2 to M phase was blocked. On the other hand, incubation of bloodstream forms with 1 microM **lactacystin** led to arrest of 30-35% of the cell population in G1 and 55-60% of the cells in G2, indicating that both transition from G1 to S and from G2 to M were blocked. These observations were also confirmed by using another inhibitor of proteasome, N-carbobenzoxy-L-leucyl-L-leucyl-L-norvalinal (LLnV), which arrested procyclic forms in G2, and bloodstream forms in both G1 and G2. These results suggest that proteasome activity is essential for driving cell cycle progression in T. brucei, and that proteasomes may control cellular functions differently in bloodstream and procyclic forms of T. brucei.

ACCESSION NUMBER: 1998135663 MEDLINE
DOCUMENT NUMBER: 98135663 PubMed ID: 9476796

TITLE: **Inhibition** of proteasome activity blocks cell cycle progression at specific phase boundaries in African trypanosomes.

AUTHOR: Mutomba M C; To W Y; Hyun W C; Wang C C
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of California San Francisco, 94143-0446, USA.. mutomba@cgl.ucsf.edu

CONTRACT NUMBER: AI-21786 (NIAID)
SOURCE: MOLECULAR AND BIOCHEMICAL PARASITOLOGY, (1997 Dec 15) 90 (2) 491-504.
Journal code: 8006324. ISSN: 0166-6851.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980407
Last Updated on STN: 20000303
Entered Medline: 19980323

L4: Entry 6 of 37 File: USPT Oct 8, 2002

DOCUMENT-IDENTIFIER: US 6462019 B1
TITLE: Inhibitors of proteasomal activity and production for stimulating bone growth

Detailed Description Text (9):
In addition to the copolymers and carriers noted above, the biodegradable films and matrices may include other active or inert components. Of particular interest are those agents that promote tissue growth or infiltration, such as growth factors. Exemplary growth factors for this purpose include epidermal growth factor (EGF), fibroblast growth factor (FGF), platelet-derived growth factor (PDGF), transforming growth factors (TGFs), parathyroid hormone (PTH), leukemia inhibitory factor (LIF), insulin-like growth factors (IGFs) and the like. Agents that promote bone growth, such as bone morphogenetic proteins (U.S. Pat. No. 4,761,471; PCT Publication WO90/11366), osteogenin (Sampath et al. Proc. Natl. Acad. Sci. USA (1987) 84:7109-13) and NaF (Tencer et al. J Biomed. Mat. Res. (1989) 23: 571-89) are also preferred. Biodegradable films or matrices include calcium sulfate, tricalcium phosphate, hydroxyapatite, polylactic acid, polyanhydrides, bone or dermal collagen, pure proteins, extracellular matrix components and the like and combinations thereof. Such biodegradable materials may be used in combination with non-biodegradable materials, to provide desired mechanical, cosmetic or tissue or matrix interface properties.

Detailed Description Text (14):
Preparations for topical and local application comprise aerosol sprays, lotions, gels and ointments in pharmaceutically appropriate vehicles which may comprise lower aliphatic alcohols, polyglycols such as glycerol, polyethylene glycol, esters of fatty acids, oils and fats, and silicones. The preparations may further comprise antioxidants, such as ascorbic acid or tocopherol, and preservatives, such as p-hydroxybenzoic acid esters.

Detailed Description Text (18):
The liposomes may be made from the present compounds in combination with any of the conventional synthetic or natural phospholipid liposome materials including phospholipids from natural sources such as egg, plant or animal sources such as phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol, sphingomyelin, phosphatidylserine, or phosphatidylinositol and the like. Synthetic phospholipids that may also be used, include, but are not limited to: dimyristoylphosphatidylcholine, dioleoylphosphatidylcholine, dipalmitoylphosphatidylcholine and distearoylphosphatidycholine, and the corresponding synthetic phosphatidylethanolamines and phosphatidylglycerols. Cholesterol or other sterols, cholesterol hemisuccinate, glycolipids, cerebrosides, fatty acids, gangliosides, sphingolipids, 1,2-bis(oleoyloxy)-3-(trimethyl ammonio) propane (DOTAP), N-[1-(2,3-dioleoyl) propyl-N,N,N-trimethylammonium chloride (DOTMA), and other cationic lipids may be incorporated into the liposomes, as is known to those skilled in the art. The relative amounts of phospholipid and additives used in the liposomes may be varied if desired. The preferred ranges are from about 60 to 90 mole percent of the phospholipid; cholesterol, cholesterol hemisuccinate, fatty acids or cationic lipids may be used in amounts ranging from 0 to 50 mole percent. The amounts of the present compounds incorporated into the lipid layer of liposomes can be varied with the concentration of the lipids ranging from about 0.01 to about 50 mole percent.

Detailed Description Text (29):

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Search Results - Record(s) 1 through 10 of 37 returned.

☐ 1. Document ID: US 6566553 B2

L4: Entry 1 of 37 File: USPT May 20, 2003

US-PAT-NO: 6566553
DOCUMENT-IDENTIFIER: US 6566553 B2

TITLE: Synthesis of clasto-lactacystin .beta.-lactone and analogs thereof

DATE-ISSUED: May 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Soucy; Fran.cedilla.ois	Arlington	MA		
Plamondon; Louis	Watertown	MA		
Behnke; Mark	Somerville	MA		
Roush; William	Ann Arbor	MI		

US-CL-CURRENT: 564/123; 544/176, 546/245, 548/215, 548/240, 548/540, 564/133

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6534277 B1

L4: Entry 2 of 37 File: USPT Mar 18, 2003

US-PAT-NO: 6534277
DOCUMENT-IDENTIFIER: US 6534277 B1

TITLE: Method for identifying a compound to be tested for an ability to reduce immune rejection by determining Stat4 and Stat6 proteins

DATE-ISSUED: March 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hancock; Wayne William	Medfield	MA		
Ozkaynak; Engin	Milford	MA		

US-CL-CURRENT: 435/7.1; 435/6, 436/501

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 3. Document ID: US 6515197 B1

L4: Entry 3 of 37 File: USPT Feb 4, 2003

US-PAT-NO: 6515197
DOCUMENT-IDENTIFIER: US 6515197 B1

TITLE: Transgenic mouse expressing a polynucleotide encoding a human ataxin-2 polypeptide

DATE-ISSUED: February 4, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Pulst; Stefan M.	Los Angeles	CA		
Huynh; Duong P.	Long Beach	CA		

US-CL-CURRENT: 800/18; 435/29, 435/320.1, 435/354, 536/23.5, 800/3, 800/8

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 4. Document ID: US 6492333 B1

L4: Entry 4 of 37 File: USPT Dec 10, 2002

US-PAT-NO: 6492333
DOCUMENT-IDENTIFIER: US 6492333 B1

TITLE: Treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mundy; Gregory R.	San Antonio	TX		

US-CL-CURRENT: 514/18; 514/12, 514/13, 514/613, 514/617

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 6485955 B1

L4: Entry 5 of 37 File: USPT Nov 26, 2002

US-PAT-NO: 6485955
DOCUMENT-IDENTIFIER: US 6485955 B1

TITLE: Quiescent cell dipeptidyl peptidase: a novel cytoplasmic serine protease

DATE-ISSUED: November 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Huber; Brigitte T.	Cambridge	MA		
Underwood; Robert H.	Quincy	MA		

US-CL-CURRENT: 435/219; 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 6. Document ID: US 6462019 B1

L4: Entry 6 of 37 File: USPT Oct 8, 2002

US-PAT-NO: 6462019
DOCUMENT-IDENTIFIER: US 6462019 B1

TITLE: Inhibitors of proteasomal activity and production for stimulating bone growth

DATE-ISSUED: October 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mundy; Gregory R.	San Antonio	TX		
Garrett; I. Ross	San Antonio	TX		
Rossini; G.	San Antonio	TX		

US-CL-CURRENT: 514/12; 435/69.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 7. Document ID: US 6458825 B1

L4: Entry 7 of 37 File: USPT Oct 1, 2002

US-PAT-NO: 6458825
DOCUMENT-IDENTIFIER: US 6458825 B1

TITLE: Lactacystin analogs

DATE-ISSUED: October 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fenteany; Gabriel	Cambridge	MA		
Jamison; Timothy F.	Cambridge	MA		
Schreiber; Stuart L.	Boston	MA		
Standaert; Robert F.	Arlington	MA		

US-CL-CURRENT: 514/421; 514/444, 514/470

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 8. Document ID: US 6451994 B1

L4: Entry 8 of 37 File: USPT Sep 17, 2002

US-PAT-NO: 6451994
DOCUMENT-IDENTIFIER: US 6451994 B1
**** See image for Certificate of Correction ****

TITLE: 23413, a novel human ubiquitin protease

DATE-ISSUED: September 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kapeller-Libermann; Rosana	Chestnut Hill	MA		
Hunter; John Joseph	Somerville	MA		

US-CL-CURRENT: 536/23.5; 536/23.1, 536/24.3, 536/24.31

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 9. Document ID: US 6410512 B1

L4: Entry 9 of 37 File: USPT Jun 25, 2002

US-PAT-NO: 6410512
DOCUMENT-IDENTIFIER: US 6410512 B1

TITLE: Inhibitors of proteasomal activity for stimulating hair growth

DATE-ISSUED: June 25, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mundy; Gregory R.	San Antonio	TX		
Garrett; I. Ross	San Antonio	TX		
Rossini; G.	San Antonio	TX		

US-CL-CURRENT: 514/12; 514/880

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
Draw Desc | Image

☐ 10. Document ID: US 6403646 B1

L4: Entry 10 of 37 File: USPT Jun 11, 2002

US-PAT-NO: 6403646

DOCUMENT-IDENTIFIER: US 6403646 B1
**** See image for Certificate of Correction ****

TITLE: Method for the treatment of alpha-1-antitrypsin deficiency and related pathologies

DATE-ISSUED: June 11, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Perlmutter; David H.	Pittsburgh	PA	15213	
Burrows; Jon A. J.	St. Louis	MO	63110	
Willis; Lauren K.	Norfolk	VA	23510-1001	
Teckman; Jeffery H.	St. Louis	MO	63110	

US-CL-CURRENT: 514/570; 514/568, 514/569

BMP promoter-active compounds can be examined in a variety of other assays that test specificity and toxicity. For instance, non-BMP promoters or response elements can be linked to a reporter gene and inserted into an appropriate host cell. Cytotoxicity can be determined by visual or microscopic examination of BMP promoter- and/or non-BMP promoter-reporter gene-containing cells, for instance. Alternatively, nucleic acid and/or protein synthesis by the cells can be monitored. For in vivo assays, tissues may be removed and examined visually or microscopically, and optionally examined in conjunction with dyes or stains that facilitate histologic examination. In assessing in vivo assay results, it may also be useful to examine biodistribution of the test compound, using conventional medicinal chemistry/animal model techniques.

Detailed Description Text (31):
An assay for bone resorption or bone formation is similar to that described by Gowen M. & Mundy G. J Immunol (1986) 136:2478-82. Briefly, four days after birth, the front and parietal bones of ICR Swiss white mouse pups are removed by microdissection and split along the sagittal suture. In an assay for resorption, the bones are incubated in BGJb medium (Irvine Scientific, Santa Ana, Calif.) plus 0.02% (or lower concentration) .beta.-methylcyclodextrin, wherein the medium also contains test or control substances. The medium used when the assay is conducted to assess bone formation is Fitton and Jackson Modified BGJ Medium (Sigma) supplemented with 6 .mu.g/ml insulin, 6 .mu.g/ml transferrin, 6 ng/ml selenous acid, calcium and phosphate concentrations of 1.25 and 3.0 mM, respectively, and ascorbic acid to a concentration of 100 .mu.g/ml is added every two days. The incubation is conducted at 37.degree. C. in a humidified atmosphere of 5% CO.sub.2 and 95% air for 96 hours.

Detailed Description Text (50):
MG-63 cells are grown in confluency in alpha MEM media and 10% fetal calf serum (FCS). Cells are then treated for 24 hours with specific compounds. Following the indicated treatments, cells are scraped with a disposable scraper, washed twice with phosphate saline solution (137 mM NaCl, 10 mM d-glucose, 4 mM KCl, 0.5 mM Na.sub.2 HPO.sub.4, 0.1 mM KH.sub.2 PO.sub.4), centrifuged, and the resulting pellet is suspended in the sample buffer containing 2% SDS, pH 6.75. The samples are heated and the concentration of total protein calculated by means of Micro bicinchoninic acid (BCA) Protein Assay Kit (Pierce, Rockford, Ill./USA). The samples are diluted to obtain a final protein concentration of 2 mg/ml, supplemented with 10% 2-mercaptoethanol, 1% bromophenol blue and run on a 4-15% SDS-PAGE. Resulting gels are Western blotted with anti-ubiquitin rabbit polyclonal antibody (diluted 1:100; Sigma, St. Louis, Mo./USA). The samples are visualized with horse-radish peroxidase coupled anti-rabbit IgG antibodies (Amersham Corp., Arlington Heights, Ill./USA) using ECL detection kits (Amersham Corp.).

Detailed Description Text (52):
The probe for electrophoretic mobility shift assays is a 32P-labeled double-stranded oligonucleotide containing the consensus sequence specific for NF-.kappa.B (Promega). Nuclear extracts (5 ug) are pre-incubated in 20-ul reaction mixtures containing 10 mM Tris-HCl, pH 7.5, 50 mM NaCl, 2.5 mM DTT, 0.5 mM EDTA, 1 mM MgCl.sub.2, 4% glycerol, and 5 ug of poly (dI-dC). After 10 min at room temperature, 10-20 frmol of probe is added, and incubated further for 20 min. DNA-protein complexes are separated from free oligonucleotides on a 5% polyacrylamide/0.5.times.TBE gel (45 mM Tris-HCl, 45 mM boric acid, 1 mM EDTA). After electrophoresis, gels are dried and autoradiographed.

Detailed Description Text (54):
In the foregoing list, lactacystin is known to be an irreversible inhibitor of proteasome activity. It binds to the .beta. catalytic subunit and is a specific inhibitor of the 20S proteasome. It also irreversibly inhibits NF-.kappa.B.

Detailed Description Text (56):
Certain peptidyl epoxy ketones such as EST are irreversible inhibitors of the proteasomes. MG-132 shows activity against the chymotryptic activity of the 20S protein without affecting its ATPase or isopeptidase activity and reversibly inhibits NF-.kappa.B activity. MG-115 and MG-341 show similar activities to MG-132. Various other inhibitors of NF-.kappa.B are less active in the ABA assay. These

include capsaicin, curcumin, and resiniferatoxin. Other compounds known to inhibit NF-.kappa.B are gliotoxin and PDTC (1-pyrrolidine carbothiotic acid). Various other compounds such as BAY-11-7082 and BAY-11-7085 as well as calyculin-A inhibit phosphorylation of NF-.kappa.B. Calpain inhibitor inhibits calpain 1 and the proteasome; other compounds such as olomoucine and roscovitine inhibit cdk2 and/or cdk5.

Detailed Description Text (67):
The results are shown in the right-hand charts in FIGS. 1A and 1B. As shown, the control compound 59-0328, which is simvastatin, gives a good response. The known proteasome inhibitors MG-132 and MG-115 also show high activity; MG-132 is effective at lower concentrations. Positive responses are also obtained using lactacystin. However, gliotoxin, olomoucine, roscovitine, SN50, PDTC, and capsaicin do not give promising responses.

Detailed Description Text (72):
The results in Example 1 were somewhat imperfectly correlated with the results in this assay. The control compound, simvastatin showed new bone formation in this assay as did MG-132 and lactacystin. MG-115 also showed positive results although less dramatic than those of simvastatin. However, gliotoxin, which appeared negative in the ABA assay of Example 1 did demonstrate the ability to stimulate bone growth. The remaining compounds, olomoucine, roscovitine, SN50, PDTC and capsaicin appeared negative in this assay.

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Search Results - Record(s) 1 through 10 of 15 returned.

1. Document ID: US 6534277 B1

L6: Entry 1 of 15 File: USPT Mar 18, 2003

US-PAT-NO: 6534277
DOCUMENT-IDENTIFIER: US 6534277 B1

TITLE: Method for identifying a compound to be tested for an ability to reduce immune rejection by determining Stat4 and Stat6 proteins

DATE-ISSUED: March 18, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hancock; Wayne William	Medfield	MA		
Ozkaynak; Engin	Milford	MA		

US-CL-CURRENT: 435/7.1; 435/6, 436/501

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

2. Document ID: US 6492333 B1

L6: Entry 2 of 15 File: USPT Dec 10, 2002

US-PAT-NO: 6492333
DOCUMENT-IDENTIFIER: US 6492333 B1

TITLE: Treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors

DATE-ISSUED: December 10, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mundy; Gregory R.	San Antonio	TX		

US-CL-CURRENT: 514/18; 514/12, 514/13, 514/613, 514/617

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

3. Document ID: US 6485955 B1

L6: Entry 2 of 15 File: USPT Dec 10, 2002

DOCUMENT-IDENTIFIER: US 6492333 B1
TITLE: Treatment of myeloma bone disease with proteasomal and NF-.kappa.B activity inhibitors

Brief Summary Text (11):
NF-.kappa.B is a transcription factor which regulates the expression of the kappa light chain gene in murine B lymphocytes, but is now known to be expressed ubiquitously. A number of different NF-.kappa.B proteins have been identified and well-characterized (Siebenlist et al. Annu Rev Cell Biol (1994) 10:405-455; see also, Baeurele et al. Cell (1996) 87:13-20). NF-.kappa.B in its active state is a heterodimer, which consists usually of two subunits. The most common subunits are known as P65 and P50; another common subunit is P52. Different combinations of these subunits may be involved in the observation of different target genes. In unstimulated cells, NF-.kappa.B is both present in the cytoplasm and bound to other proteins known as IkB.alpha. and IkB.beta. and prevent it from entering the nucleus. Upon stimulation of cells, specific enzymes lead to the phosphorylation of IkB, which in turn leads to its rapid degradation in the proteasomes. Upon degradation of IkB, NF-.kappa.B is then available to translocate to the nucleus. In the nucleus, NF-.kappa.B binds to promoter sequences of target genes and leads to their transcription. Proteasome activity is thus required for NF-.kappa.B translocation.

Brief Summary Text (29):
In the foregoing list, lactacystin is known to be an irreversible inhibitor of proteasome activity. It binds to the .beta. catalytic subunit and is a specific inhibitor of the 20S proteasome. It also irreversibly inhibits NF-.kappa.B.

Brief Summary Text (31):
Certain peptidyl epoxy ketones such as EST are irreversible inhibitors of the proteasomes. MG-132 shows activity against the chymotryptic activity of the 20S protein without affecting its ATPase or isopeptidase activity and reversibly inhibits NF-.kappa.B activity. MG-115 and MG-341 show similar activities to MG-132. Various other inhibitors of NF-.kappa.B are less active in the ABA assay. These include capsaicin, curcumin, and resiniferatoxin. Other compounds known to inhibit NF-.kappa.B are gliotoxin and PDTC (1-pyrrolidine carbothiotic acid). Various other compounds such as BAY-11-7082 and BAY-11-7085 as well as calyculin-A inhibit phosphorylation of NF-.kappa.B. Calpain inhibitor inhibits calpain 1 and the proteasome; other compounds such as olomoucine and roscovitine inhibit cdk2 and/or cdk5.

L6: Entry 3 of 15 File: USPT Nov 26, 2002

US-PAT-NO: 6485955
DOCUMENT-IDENTIFIER: US 6485955 B1

TITLE: Quiescent cell dipeptidyl peptidase: a novel cytoplasmic serine protease

DATE-ISSUED: November 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Huber; Brigitte T.	Cambridge	MA		
Underwood; Robert H.	Quincy	MA		

US-CL-CURRENT: 435/219; 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. Desc | Image

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☐ 4. Document ID: US 6458825 B1

L6: Entry 4 of 15 File: USPT Oct 1, 2002

US-PAT-NO: 6458825
DOCUMENT-IDENTIFIER: US 6458825 B1

TITLE: Lactacystin analogs

DATE-ISSUED: October 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fenteany; Gabriel	Cambridge	MA		
Jamison; Timothy F.	Cambridge	MA		
Schreiber; Stuart L.	Boston	MA		
Standaert; Robert F.	Arlington	MA		

US-CL-CURRENT: 514/421; 514/444, 514/470

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC | Draw. Desc | Image

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☐ 5. Document ID: US 6451994 B1

L6: Entry 5 of 15 File: USPT Sep 17, 2002

US-PAT-NO: 6451994
DOCUMENT-IDENTIFIER: US 6451994 B1
**** See image for Certificate of Correction ****

TITLE: 23413, a novel human ubiquitin protease

DATE-ISSUED: September 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kapeller-Libermann; Rosana	Chestnut Hill	MA		
Hunter; John Joseph	Somerville	MA		

US-CL-CURRENT: 536/23.5; 536/23.1, 536/24.3, 536/24.31

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 6. Document ID: US 6335358 B1

L6: Entry 6 of 15 File: USPT Jan 1, 2002

US-PAT-NO: 6335358
DOCUMENT-IDENTIFIER: US 6335358 B1
**** See image for Certificate of Correction ****

TITLE: Lactacystin analogs

DATE-ISSUED: January 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fenteany; Gabriel	Cambridge	MA		
Jamison; Timothy F.	Cambridge	MA		
Schreiber; Stuart L.	Boston	MA		
Standaert; Robert F.	Arlington	MA		

US-CL-CURRENT: 514/412; 514/192, 514/210.05, 514/210.06, 514/414, 514/422, 514/424, 514/428, 514/439, 514/441, 514/443, 514/444, 514/464, 514/465, 514/466

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 7. Document ID: US 6329171 B1

L6: Entry 7 of 15 File: USPT Dec 11, 2001

US-PAT-NO: 6329171
DOCUMENT-IDENTIFIER: US 6329171 B1
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TITLE: 23484, A novel human ubiquitin protease

DATE-ISSUED: December 11, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kapeller-Libermann; Rosana	Chestnut Hill	MA		

US-CL-CURRENT: 435/69.1; 435/252.3, 435/325, 435/455, 435/471, 536/23.1, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 8. Document ID: US 6287569 B1

L6: Entry 8 of 15 File: USPT Sep 11, 2001

US-PAT-NO: 6287569
DOCUMENT-IDENTIFIER: US 6287569 B1

TITLE: Vaccines with enhanced intracellular processing

DATE-ISSUED: September 11, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kipps; Thomas J.	Ranchos Santa Fe	CA		
Wu; Yunqi	San Diego	CA		

US-CL-CURRENT: 424/199.1; 424/204.1, 435/235.1, 435/320.1, 435/325, 435/343.2, 536/23.2, 536/23.4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 9. Document ID: US 6235481 B1

L6: Entry 9 of 15 File: USPT May 22, 2001

US-PAT-NO: 6235481
DOCUMENT-IDENTIFIER: US 6235481 B1
**** See image for Certificate of Correction ****

TITLE: Polynucleotides encoding calpain 10

DATE-ISSUED: May 22, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Horikawa; Yukio	Kobe			JP
Oda; Naohisa	Nagoya			JP
Hanis; Craig L.	Houston	TX		
Bell; Graeme I.	Chicago	IL		
Cox; Nancy J.	Inverness	IL		

US-CL-CURRENT: 435/6; 536/23.1, 536/24.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | KWIC
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☐ 10. Document ID: US 6214862 B1

L6: Entry 10 of 15 File: USPT Apr 10, 2001

US-PAT-NO: 6214862
DOCUMENT-IDENTIFIER: US 6214862 B1
**** See image for Certificate of Correction ****

TITLE: Lactacystin analogs

DATE-ISSUED: April 10, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fenteany; Gabriel	Cambridge	MA		
Jamison; Timothy F.	Cambridge	MA		
Schreiber; Stuart L.	Boston	MA		
Standaert; Robert F.	Arlington	MA		

US-CL-CURRENT: 514/423; 514/365, 514/369, 514/370, 514/371, 514/376, 514/377, 514/439, 514/440, 514/441, 514/445, 514/446, 514/448, 514/452, 514/473

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